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# Exercise, Exercise Training, and the Immune System

## A Compendium of Research (1902-1991)

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A.J. Hardesty, J.E. Greenleaf, S. Simonson, A. Hu,  
and C.G.R. Jackson

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(NASA-TM-108778) EXERCISE,  
EXERCISE TRAINING, AND THE IMMUNE  
SYSTEM. A COMPENDIUM OF RESEARCH  
(1902-1991) (NASA) 167 p

N94-23575

Unclass

November 1993

G3/52 0203558

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# **Exercise, Exercise Training, and the Immune System**

## **A Compendium of Research (1902-1991)**

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November 1993



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## Summary

This compendium includes abstracts and synopses of clinical observations and of more basic studies involving physiological mechanisms concerning interaction of physical exercise and the human immune system. If the author's abstract or summary was appropriate, it was included. In other cases a more detailed synopsis of the

paper was prepared under the subheadings Purpose, Methods, Results and Conclusions. Author and subject indices are provided, plus a selected bibliography of related work or those papers received after the volume was being prepared for publication. This volume includes material published from 1902 through 1991.

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## Introduction

The purpose of this compendium is to present summaries of clinical observations and results from more basic studies that help to elucidate physiological mechanisms of the interaction of physical exercise and exercise conditioning on the human immune system. If the author's abstract or summary was appropriate, it was utilized. In some cases a more detailed synopsis was provided under the subheadings Purpose, Methods, Results, and Conclusions.

This volume includes studies published from 1902 through 1991. Author and subject indices are provided.

The material is listed in alphabetical order by first author and numbered consecutively by abstract number, not page number.

We thank our many colleagues who sent us reprints, and apologize to those whose work we have inadvertently overlooked.

The authors thank Becky Werner and Robert Farrell for valuable technical assistance.



## Abstracts and Synopses

### 1. Aarstad, H.J., G. Gaudernack, and

R. Seljelid:

Stress causes reduced natural killer activity in mice.  
*Scandinavian Journal of Immunology* 18:461-464,  
1983.

#### Authors' abstract

The natural killer (NK) activity of spleen cells from C57B1/10 mice subjected to standardized stress conditions was reduced when compared with that of untreated controls. Both the total number of nucleated spleen cells and their cytotoxic activity against an NK-sensitive target were reduced throughout an 8-day stress period.

### 2. Abbott, A.C. and N. Gildersleeve:

The influence of muscular fatigue and of alcohol upon certain of the normal defences.

*University of Pennsylvania Medical Bulletin*  
23:169-181, 1910.

#### Synopsis

##### Purpose

1. To determine the effect of severe muscular exertion on both the cellular and opsonic contents of the blood.
2. To discover to what extent such fluctuations as might occur are accompanied by variations in the susceptibility of the animal to infections under consideration.

##### Methods

1. The blood of 18 normal rabbits was examined for the number of white blood cells and for its opsonizing powers.
2. These rabbits were then run in a revolving drum that was made of reinforced galvanized iron netting, swung in a frame on axles, and revolved by an electric motor.
3. Each rabbit was forced to do muscular exercise for varying lengths of time.
4. Diluted alcohol was passed by means of a lubricated soft rubber catheter directly into the stomach.
5. Certain rabbits were inoculated with either *Streptococcus pyogenes* or *Staphylococcus pyogenes*.

##### Results

1. The opsonizing power of the blood, as determined by the opsonic index, may be markedly diminished by severe muscular exercise and by the ingestion of alcohol.

2. There was reduction from 25% to 60% in the opsonic index of the fatigued rabbits, and an increase from 20% to 100+ % in the number of white cells in the peripheral blood.

3. The ingestion of alcohol is quickly accompanied by a lowered opsonic index, but the index quickly returns to normal with cessation of alcohol ingestion. The amount of alcohol needed to bring out this result had no influence on the resistance of the animal to infection.

4. Though the opsonic content is diminished as a result of severe muscular exercise, there is a coincident temporary increase of the leukocytic content of peripheral blood which may return to normal if exercise is continued.

5. Prolonged muscular exercise followed by injection of pyogenic bacteria may favor pyogenic infections.

6. Violent muscular exercise following inoculation is more apt to have serious results than that preceding it. This is significant in its bearing upon the observation noted in the opening paragraph of this communication.

#### Conclusions

1. Factors other than those considered here are involved in the condition of susceptibility and immunity in so far as they relate to infection by the pyogenic organisms.
2. Some of our failures to infect animals in these experiments may perhaps be explained by the marked temporary increase in the leukocyte content of the peripheral blood.

### 3. Ahlborg, B.:

Leukocytes in blood during prolonged physical exercise.

*Forsvarsmedicin* 2:36-48, 1967.

#### Author's synopsis

The present study shows that the resting leukocyte level has not been reached 1 hour after the end of exercise. Earlier it has been reported that the leukocytosis caused by exercise of 10 minutes duration had receded to the resting value 90 minutes after the end of exercise. The situation thus appears to be that the rapid increase in number of leukocytes in the blood as a result of exercise returns to resting values slowly after the end of exercise and in accordance with a falling exponential function. One measure of relative work load used in this study has been the pulse rate after 10 minutes of exercise. This measure provides sufficient information for evaluating the

individual relative load. As has been demonstrated in the present study absolute as well as relative work load is correlated to the total leukocyte count at the end of exercise. Much higher correlations are reported between work time and total leukocyte count. Between work load and work time there is naturally some relationship for each individual which might explain that also work load in the present study is correlated to total leukocyte count. As a matter of fact i.e., the relative work load, expressed as 10-minute pulse rate, is negatively correlated to work time ( $r = 0.48, p < 0.001$ ). The higher correlations with work time than with work load support that exercise leukocytosis is influenced rather by time than by intensity of work.

#### **4. Ahlborg, B. and G. Ahlborg:**

Exercise leukocytosis with and without beta-adrenergic blockade.  
*Acta Medica Scandinavica* 187:241-246, 1970.

##### **Authors' abstract**

Exercise leukocytosis during standardized work has been demonstrated in eight male healthy test subjects. Mostly the leukocytosis was due to an increase in segmented neutrophils, to a minor degree an increase in lymphocytes. After propranolol (Inderal®) administration exercise results in practically no increase in neutrophil leukocytes or lymphocytes. Exercise leukocytosis is concluded—at least partly—to be mediated by a beta-receptor mechanism.

#### **5. Albrecht, R.M. and F.B. Locke:**

Effect of physical activity on prognosis of poliomyelitis.

*Journal of the American Medical Association*  
146:769-771, 1951.

##### **Synopsis**

**Purpose** To determine whether the severity of poliomyelitis could be ascribed largely to the extent of physical activity at the time of illness.

##### **Methods**

1. A detailed history of symptoms and of the physical activities from 3 days before the onset was taken from each of 200 poliomyelitis patients aged 3 years or more.
2. Physical activities, categorized as bed rest, light activity, normal activity, and heavy activity, were rated by someone uninformed of the extent of the paralysis of the patient at the time of the rating.

3. All patients were muscle-graded by trained physiotherapists between 5.5 months and 7 months after the onset of the illness, according to the standard form used by the New York State Department of Health.

##### **Results**

1. Deaths and severe paralysis in children are not related to the degree of physical activity either shortly before the onset of illness or at any time during the illness.
2. Deaths and severe paralysis in adults may be attributed in part to the degree of physical activity in the meningial stage.

#### **6. Alluisi E.A., W.R. Beisel, B.B. Morgan, Jr., and L.S. Caldwell:**

Effects of sandfly fever on isometric muscular strength, endurance, and recovery.

*Journal of Motor Behavior* 12: 1-11, 1980.

##### **Authors' abstract**

The isometric muscular strength and endurance of 10 male volunteers were measured four times per day for 15 consecutive days. Eight experimental subjects were inoculated with sandfly fever virus and two double-blind controls were given sterile saline on the seventh day. The muscular performances of the control subjects remained essentially constant throughout. Decrements in muscular strength and endurance occurred with the experimental subjects during the brief period of illness three or four days after inoculation, then performances improved towards baseline levels. Although the performance decrements occurred in conjunction with changes in certain metabolic indicators of the internal biochemical state of the skeletal muscles, the recovery occurred while these were still abnormal.

#### **7. Altschule, M.D., L.H. Altschule, and**

**K.J. Tillotson:**

Changes in leukocytes of the blood in man after electrically induced convulsions.

*Archives of Neurology and Psychiatry* 62:624-629, 1949.

##### **Synopsis**

**Purpose** To study the number of circulating lymphocytes and other leukocytes before and after such seizures.

## Methods

1. Thirteen patients from 19 to 71 years were given shock treatments either 3 times a week or at 5 to 7 minute intervals.
2. Blood was drawn from an antecubital vein 1 to 3 minutes before the induction of the seizure and again 1/2 hour and 3 hours after the seizure.

## Results

1. Immediately before convulsion, leukocyte counts averaged 10,064 cells per cubic ml. One half hour after convulsion the counts averaged -422 cells per cubic ml from the control (before convulsion). Three hours after convulsion the count averaged +2,060 cells per cubic ml from the control.
2. Before convulsion the polymorphonuclear cell counts averaged 7,360 cells per cubic ml. One half hour after convulsion counts averaged -19 cells per cubic ml from the control. Three hours after convulsion, counts averaged +2,667 cells per cubic ml from the control.
3. Before convulsion lymphocyte counts averaged 2,200 cells per cubic ml. One half hour after convulsion counts averaged -503 cells per cubic ml difference from the control. Three hours after convulsion counts averaged -733 cells per cubic ml from the control.

## Conclusions

1. After electrically induced convulsions in psychotic patients a rapid and sustained fall in blood lymphocytes develops; late rises in polymorphonuclear cells and in the total leukocyte count also occur.
2. The changes observed are consistent with the effects of increased adrenal cortex hormones.

## 8. Andersen, K.L.:

Leukocyte response to brief, severe exercise.  
*Journal of Applied Physiology* 7:671-674, 1955.

### Author's abstract

The leukocyte response to brief severe exercise was determined in 13 healthy men. Three of the subjects were also studied during a 2-hour recovery period. The results show briefly: a) The exercise leukocytosis ranged from 27-131% of the pre-exercise values. A tendency was observed for the total number of leukocytes and the number of lymphocytes and monocytes to increase concomitantly with increasing running time. b) A peak in the leukocytosis was reached 15 minutes after termination of the run; 30-60 minutes after exercise the pre-exercise level was reached, and in one subject it dropped below

this value. At the end of the recovery period studied, a slight leukocytosis was observed. c) The lymphocytosis changed to lymphopenia during the recovery period. The monocytes followed a pattern similar to the lymphocytes. d) No significant changes were observed in the number of neutrophilic granulocytes immediately after exercise. During the recovery period, an increased number of neutrophils were observed. The eosinophils followed a pattern similar to the lymphocytes.

## 9. Andrianopoulos, G., R.L. Nelson,

C.T. Bombeck, and G. Souza:

The influence of physical activity in 1,2 dimethylhydrazine induced colon carcinogenesis in the rat.  
*Anticancer Research* 7:849-852, 1987.

### Authors' abstract

Recent epidemiologic findings indicate that relative risk of colon cancer is augmented with increasing proportion of time spent on sedentary occupations, and reduced with occupations requiring high levels of work-related physical activity. Therefore, the influence of exercise on experimental colon carcinogenesis was investigated. Spontaneous running wheel activity was related to incidence of 1,2 dimethylhydrazine (DMH) colon tumor induced in Colon tumor incidence was significantly reduced in animals that were allowed spontaneous wheel activity throughout the period of DMH tumor induction vs. standard housed controls ( $p < 0.05$ ), indicating that, in the rat, physical activity protects against colon tumorigenesis. Further comparisons reveal a mild positive association ( $p = 0.07$ ) between activity and incidence of tumors in the left colon. These results are in accord with epidemiologic findings indicating reduced colon cancer risk with increased physical activity. Possible mechanisms for the protective influence of physical activity on tumorigenesis include reduction in fecal pH, body weight and increased antioxidant enzyme activity. To the extent that epidemiologic associations between colon cancer and activity are inclusive of the multidimensional nature of physical activity, animal models such as that utilized in this experiment can be utilized for investigating the etiologic potential, or strength of association in variables that have been epidemiologically associated with colon cancer risk.



**10. Antoni, M.H., A. LaPerriere,**

**N. Schneiderman, and M.A. Fletcher:**

Stress and immunity in individuals at risk for AIDS.  
*Stress Medicine* 7:35-44, 1991.

**Authors' abstract**

We have examined psychosocial and immune system stress responses in gay men before and after their notification of human immunodeficiency virus (HIV-1) status and as a consequence of stress management intervention procedures. Prior to notification, early stage, asymptomatic, seropositive men displayed compromised immunity as evidenced by significant decreases in CD4+ cell number, the helper subset (CD29+CD4+), CD4+/CD8+ ratio, and lymphocyte responses to mitogens. Prior to diagnosis, both seronegative and seropositive men revealed suppression of NK cell cytotoxicity and mitogen responsiveness relative to matched laboratory control subjects not awaiting diagnosis. Immune suppression in these seronegative men disappeared after diagnosis, indicating its relationship to anticipation of serostatus notification. We also found that a 10-week program of aerobic exercise or psychosocial stress management buffered the psychological impact of notification of seropositivity. The aerobic exercise program produced significant increases in CD4+ and NKH.1+ for seronegatives and CD45R+CD4+ cell number and mitogen responsiveness for seropositives. We are assessing our interventions as tools for retarding immune deterioration and disease progression in HIV-1 seropositive individuals.

**11. Asgeirsson, G. and J.A. Bellanti:**

Exercise, immunology, and infection.  
*Seminars in Adolescent Medicine* 3:199-203, 1987.

**Authors' synopsis**

There is no doubt that exercise (possibly through mechanisms similar to stress) has a major effect on the immune response. It seems clear that strenuous exercise during the incubation of certain viral diseases, notably poliomyelitis, greatly increases the incidence and severity of complications, such as paralysis. It is not quite as clear, however, whether exercising makes one more (or less) susceptible to infection. Most articles reviewed suggested that exercise may suppress immune function, thereby making the athlete more infection prone. All of these studies examined biochemical changes induced by exercise and did not attempt a clinical correlation. All of the clinical papers supporting this view are either case reports or studies with a limited number of participants observed over short periods. Many reports about disease outbreaks occurred in athletes on school teams. It is well

known that crowding may increase the incidence of infection, which may well apply here, and may also partly explain the experience of the Olympic team's physicians. The outbreaks of skin infections discussed above are almost definitely the result of the close contact involved in those sports.

**12. Bailey, F., C.M. Maresch, J.R. Hoffman,**

**C.L. Gabaree, D. Hannon,**

**M.R. Deschenes, A. Abraham,**

**W.J. Kraemer, L.E. Armstrong:**

Immune factor responses to Wingate anaerobic power testing.

*Medicine and Science in Sports and Exercise* 23:S62, 1991.

**Authors' abstract**

Acute exercise apparently stimulates the immune system, but little is known about the effects of short-term high-intensity exercise on those responses. The present study examined the response of selected hematologic factors, related to the immune system, to the 30 sec Wingate Anaerobic Power test. Eleven active males ( $20.1 \pm 1.4$  yr), familiar with Wingate testing, volunteered to perform 4 tests (each separated by 7 days), but otherwise maintained their normal activity patterns. Venous blood was sampled, via cannula, before and within 30 sec of cessation of exercise. Subjects demonstrated no change in peak power ( $874 \pm 146$  W), mean power ( $675 \pm 89$  W) or peak plasma lactate ( $13.2 \pm 1.7$  mmol  $\cdot$  L<sup>-1</sup>) across the 4 tests. Similarly, the hematologic factors showed very reproducible responses to the 4 exercise tests. Average pre- to post-exercise values, respectively, were: WBC's,  $6.3 \pm 1.4$  vs  $9.8 \pm 1.9 \times 10^3$ /cu. mm; polymorphs,  $56.0 \pm 10.2$  vs  $47.2 \pm 11.3\%$ ; lymphocytes,  $33.3 \pm 8.9$  vs  $41.5 \pm 9.4\%$ ; eosinophils,  $2.9 \pm 1.9$  vs  $2.6 \pm 1.6\%$ ; basophils,  $0.9 \pm 0.5$  vs  $0.6 \pm 0.3\%$ ; monocytes,  $5.6 \pm 1.5$  vs  $5.2 \pm 1.6\%$ ; and platelet count,  $239.4 \pm 52.8$  vs  $275.4 \pm 58.7 \times 10^3$ /cu mm. The exercise-induced increase ( $p < 0.05$ ) in WBCs ( $35.4 \pm 5.9\%$ ) and lymphocytes ( $19.7 \pm 4.9\%$ ), and the decrease ( $p < 0.05$ ) in polymorphs ( $15.8 \pm 3.9\%$ ), could not be fully accounted for by the  $-14.5 \pm 2.2\%$  change in plasma volume. Thus, 30 sec of high-intensity exercise resulted in significant and rapid responses of selected hematologic factors related to the immune system.

### 13. Bailey, G.H.:

The effect of fatigue upon the susceptibility of rabbits to intratracheal injections of type I pneumococcus. *American Journal of Hygiene* 5:175-185, 1925.

#### Synopsis

**Purpose** To determine the effect of fatigue upon the susceptibility of rabbits to type I pneumococcus infection.

#### Methods

1. One hundred and seventy rabbits were injected intratracheally with pneumococcus I. Of these, 80 were controls and 90 were fatigued.
2. Experiments I-XI: Sixty rabbits were fatigued until exhaustion for one period only. Of these, 39 were fatigued before injection, 21 after injection, and 50 controls were used.
3. Experiments XII-XIV: In a group of 30 rabbits, 5 were fatigued two times before injection, 5 twice after injection, and 5 three times after injection. 15 controls were used.
4. Experiments XV-XVII: In a group of 30 rabbits, 10 were fatigued 6 times on alternate days over 12 days, 5 were fatigued twelve times on alternate days over 24 days, and 15 controls were used.

#### Results

1. In experiment I-XI, of those fatigued before the injection, 64.1% died. Of the 21 injected and then fatigued, 85.7% died. Of the controls, 48% died.
2. In experiment XII-XIV, 66.4% of the fatigued and 40% of controls died. Fatiguing the rabbits two to three times before or after injection increased their susceptibility to infection.

3. In experiments I-XIV, fatigue after injection was about 1.5 times as potent in lowering the resistance as fatigue which preceded injection.

4. In experiment XV-XVII, 60% of fatigued rabbits survived and only 26.7% of the controls survived.

#### Conclusions

1. One to three periods of successive fatigue in rabbits decreases their resistance to type I pneumococcus.
2. Increased susceptibility is more evident when fatigue follows injection than when injection follows fatigue.
3. Exercise training in rabbits apparently increases their resistance to type I pneumococcus.
4. More extensive pulmonary lesions occur in fatigued than in nonfatigued rabbits.

### 14. Baracos, V.E.:

Exercise inhibits progressive growth of the Morris hepatoma 7777 in male and female rats.

*Canadian Journal of Physiology and Pharmacology* 67:864-870, 1989.

#### Author's abstract

Male and female rats were either trained to swim for a 6-week period or they remained sedentary. Rats were implanted with Morris hepatoma 7777 after 3 weeks of swimming and were sacrificed after a further 3 weeks. Exercised rats of both sexes showed a significant reduction in tumor weight at sacrifice, compared with sedentary controls ( $p < 0.01$ ). Similarly, when rats were first implanted with tumors and then placed on an exercise program of 3 weeks duration, tumor growth was also reduced ( $p < 0.05$ ). These results suggest that the tumor may be sensitive to exercise at more than one point in its development. Tumor growth was inhibited to a similar extent whether the total swimming time was 10, 20, or 30h over the 3-week period. Although sedentary, tumor-bearing rats were anorexic; both male and female rats showed significant improvement of appetite during the period of tumor growth in response to exercise. Tumor implantation was associated with significant losses of whole body and muscle protein. The progression of this wasting was not significantly altered by exercise.

### 15. Baron, R.C., M.H. Hatch, K. Kleeman, and J.N. MacCormack:

Aseptic meningitis among members of a high school football team. An outbreak associated with echovirus 16 infection.

*Journal of the American Medical Association* 248:1724-1727, 1982.

#### Authors' abstract

During the period September 1 through October 1, 1978, an outbreak of enteroviral illness affected 43 (70%) of the 61 members of a high school football team. Thirty-three (54%) had symptoms of aseptic meningitis, a diagnosis confirmed for each of seven players hospitalized.

Echovirus 16 was recovered from a throat swab of one hospitalized player and from the CSF of another. Enteroviruses isolated from stool specimens taken after the illness from other ill players and from stool specimens of non-ill team members were also identified as echovirus 16. A survey among students not on the team showed an attack rate for enteroviral-like illness that was half that experienced by team members during the same period. Symptoms reported by non-team members were less severe. Only 10% had aseptic meningitis-like syndrome, and none were hospitalized. Membership on

the school football team was associated with an increased rate of illness and a greater risk for aseptic meningitis developing.

**16. Barrett, A.J., P. Longhurst, P. Sneath, and J.G. Watson:**

Mobilization of CFU-C by exercise and ACTH induced stress in man.  
*Experimental Hematology* 6:590-594, 1978.

**Authors' abstract**

This study was designed to investigate physiological factors that affect blood CFU-C numbers. Exercise was found to produce a fourfold rise in blood colony forming cells, and a twofold rise in cluster forming cells accompanied by a lymphocytosis. ACTH-induced stress caused a twofold rise in blood colony and cluster forming cells accompanied by a neutrophil leucocytosis. The results suggest that blood CFU-C exchange with a large marginal pool as well as a bone marrow pool. The procedures described could be exploited in the use of leukapheresed nucleated cells as a source of stem cells for bone marrow transplantation.

**17. Beisel, W.R., B.B. Morgan, Jr., P.J. Bartelloni, G.D. Coates,**

**F.R. DeRubertis, and E.A. Alluisi:**  
Symptomatic therapy in viral illness. A controlled study of effects on work performance.  
*Journal of the American Medical Association* 228:581-584, 1974.

**Author's abstract**

The ability to perform sustained nonphysical work is diminished during acute infectious illnesses. In this study, anticipated decrements in work performance did not occur when volunteers with experimentally induced sandfly fever were given symptomatic therapy. The therapeutic regimen, which included aspirin and propoxyphene hydrochloride administered every four hours for two days, did not entirely relieve fever or the symptoms of illness. This regimen had no detectable effect on the work performance of other noninfected volunteers included in the study as therapy controls.

**18. Bennink, M.R., H.J. Palmer, and M.J. Messina:**

Exercise and caloric restriction modify rat mammary carcinogenesis.  
*Federation Proceedings* 45:1087, 1986.

**Authors' abstract**

This study was designed to determine the effect of energy expenditure and dietary restriction on tumorigenesis. Energy balance was altered in a 2 x 2 factorial experiment by: 1) exercising rats by running on a treadmill or 2) a 16% reduction in caloric intake. Treatments were begun 24 days after initiation and continued for 160 days. Mammary cancer was initiated with 10 mg of 7,12-dimethylbenzanthracene given intragastrically. All 4 groups received the same quantity of fat, protein, vitamins, minerals and sucrose in the diet. Energy restriction (ER) was achieved by removing 15% of the corn starch from the diet fed to the ER groups. Energy content of the carcass (as a % of the ad lib., sedentary group) was: pair-fed, EX = 71; ER, EX = 61. ER decreased total body protein by 6%. EX did not change body protein. EX reduced the rate constant (rate constant is the change in tumor incidence or size with time) of the cumulative mean tumor incidence by 16% and ER reduced the rate constant by 28%. EX decreased the rate constant of the cumulative mean tumor size by 23%; however, ER increased the rate constant by 46%. In this experiment, EX was equally or more effective than ER in reducing tumorigenesis.

**19. Berg, R., O. Ringertz, and A. Espmark:**

Australia antigen in hepatitis among Swedish track-finders.  
*Acta Pathologica, Microbiologica Scandinavica* B 79:423-427, 1971.

**Authors' abstract**

An epidemic of about 600 cases of hepatitis among Swedish cross-country track-finders in 1957-1966 reported earlier was suspected, on clinical and epidemiological grounds, to be serum hepatitis. Sera from 69 of these patients, stored frozen since 1961-1962, were studied for the presence of Australia antigen. The specimens were assayed by the Ouchterlony double diffusion test and by the radial diffusion test according to Mancini et al. The results of the two tests were in good agreement. Australia antigen was found in 32 (46%) of the patients thus supporting the earlier hypothesis that the disease was a serum hepatitis. Australia antigen was found in all sera drawn within the first 9 days after onset of symptoms, the rate thereafter decreasing gradually. No specimens drawn later than 54 days after onset were

positive. In most patients with paired sera, the antigen titer dropped significantly or became negative over a 2-3 week period.

## 20. Bergmann, K.-Ch.:

Sports and allergy.  
*International Journal of Sports Medicine*  
12:S16-S18, 1991.

### Author's abstract

Allergic and asthmatic individuals may have exercise-induced respiratory problems and sports may induce, in some cases, allergic problems. Exercise-induced asthma (EIA) differs from common asthma only in its causative factor. It is a typical asthma attack following physical exercise, lasting 5-10 minutes, most often in cold and dry weather. The prevalence in asthmatic children is high, in adolescents not yet firmly established. Cold air and/or hypertonic bronchial challenges during exercise are discussed as pathophysiological mechanisms. Non-pharmacological and drug treatment of EIA must preferentially be preventative. Exercise-induced anaphylaxis (urticaria, pruritus, edema) occurs mainly in children, triggered by exercise alone or by the combination of sensitizing food and exercise. Antihistamines before exercise are recommended. The use of sport equipment can induce contact dermatitis in rare cases.

## 21. Berk, L.S., D. Nieman, S.A. Tan, S. Nehlsen-Cannarella, J. Kramer, W.C. Eby, and M. Owens:

Lymphocyte subset changes during acute maximal exercise.  
*Medicine and Science in Sports and Exercise*  
18:706, 1986.

### Authors' abstract

The purpose of this study was to determine the effects of acute maximal exercise on lymphocyte subset changes in peripheral blood. Twelve men age  $45 \pm 4.6$  ( $\bar{X} \pm SD$ ) were exercised, using the Balke protocol, to maximal exertion as determined by the 10-point Borg Scale Rating of Perceived Exertion. Blood samples were drawn from an antecubital vein 10 minutes prior to (PRE) and 15 min after (POST) exercise. Except for white blood count (WBC) and red blood count (RBC), all samples were analyzed on a laser flow cytometer for absolute lymphocyte count (ALYM), percentages of total T-lymphocytes (TL), B-lymphocytes (BL), natural killer cells (NK), helper T-lymphocytes (HT) and suppressor T-lymphocytes (ST). The ratio of HT to ST (H/S) was determined. Paired values were analyzed using the two-tailed paired t-test. Means, standard deviations, and statistical significance are given below:

These data indicate that significant lymphocyte subset changes occur with acute maximal exercise, and these changes may have varying physiological effects on immunosurveillance.

	WBC	RBC	ALYM	TL	BL	NK	HT	ST	H/S
PRE	5.7	4.3	2.4	68.7	14.2	13.0	53.8	32.7	1.94
$\pm$ SD	<u>1.3</u>	<u>0.4</u>	<u>0.5</u>	<u>10.4</u>	<u>5.1</u>	<u>4.3</u>	<u>12.6</u>	<u>11.4</u>	<u>0.9</u>
POST	7.0*	4.5*	2.9†	68.4	11.7*	22.2†	43.4†	36.4†	1.36*
$\pm$ SD	<u>2.0</u>	<u>0.3</u>	<u>0.8</u>	<u>8.4</u>	<u>3.8</u>	<u>5.9</u>	<u>10.5</u>	<u>11.1</u>	<u>0.6</u>

Units: WBC and ALYM are  $\times 10^3/\text{mm}^3$ . RBC is  $\times 10^6/\text{mm}^3$ . \*P < 0.01, †P < 0.05.

**22. Berk, L.S., D.C. Nieman, and S.A. Tan:**

Maximal exercise modifies lymphocyte subpopulations T-helper and T-suppressor and their ratio in man.

*Medicine and Science in Sports and Exercise*  
19: S43, 1987.

**Authors' abstract**

Changes in lymphocyte cell subpopulations Leu-3a (T-helper) and Leu-2a (T-suppressor) and their ratio (H/S) were studied in athletes and non-athletes in response to maximal exercise. Eleven male athletes (age 43) and nine male non-athletes (age 44) were exercised to maximal exertion (10-point Scale Rating of Perceived Exertion) using the Balke stress treadmill protocol. Peak  $\dot{V}O_2$  for athletes and non-athletes were  $54.2 \pm 1.8$  and  $33.3 \pm 1.1$  ( $\bar{X} \pm SE$ ) ml/kg/min., respectively ( $P < 0.05$ ). Blood samples were obtained 10 minutes before exercise and 15 minutes after maximal exercise. T-helper and T-suppressor percentages, and the H/S were determined by a direct immunofluorescence method. Athletes had higher pre- and post-exercise T-helper and H/S, and lower T-suppressor than non-athletes; these data showed a statistical trend with borderline significance. The T-helper were decreased and T-suppressor increased in both groups from before to after exercise ( $P < 0.05$ ). A paired one-sample t-test of the of the H/S for athletes and non-athletes from before to after exercise was decreased ( $P < 0.03$ ;  $P < 0.01$ ), respectively. These data suggest that maximal exercise can influence changes in lymphocyte subpopulations of T-helper and T-suppressor and their H/S.

**23. Berk, L.S., D.C. Nieman,**

**W.S. Youngberg, K. Arabatzis,  
M. Simpson-Westerberg, J.W. Lee,  
S.A. Tan, and W.C. Eby:**

The effect of long endurance running on natural killer cells in marathoners.

*Medicine and Science in Sports and Exercise*  
22:207-212, 1990.

**Authors' abstract**

Ten experienced marathoners were exercised 3 hours in the laboratory. Blood samples were collected at 0 hours baseline. One hour exercise and 5 minutes, 1.5 hours, 6 hours, and 21 hours recovery and were analyzed for total number of lymphocytes expressing membrane antigens found on natural killer (NK) cells. NK activity was also measured. Four of the seven subpopulations of lymphocytes studied, Leu-11<sup>+</sup>19<sup>+</sup>, Leu-11<sup>+</sup>19<sup>-</sup>, Leu-11<sup>+</sup>7<sup>-</sup>, and Leu-19<sup>+</sup>11<sup>-</sup>, showed significant within-

subject effects over time, using repeated measures ANOVA. Simple contrasts with baseline values showed that at 1.5 hours and 21 hours recovery, total number of lymphocytes bearing three different combinations of NK markers, Leu-11<sup>+</sup>19<sup>+</sup>, Leu-11<sup>+</sup>19<sup>-</sup>, and Leu-11<sup>+</sup>7<sup>-</sup>, were significantly decreased when compared with baseline values. At 1.5 hours recovery, NK activity was significantly decreased below baseline levels for four of the six effector NK cell/target K562 myelogenous leukemia cell (E:T) ratios tested. At 6 hours recovery, NK activity was still decreased significantly with the 12.5:1 and 3:1 E:T ratios. By 21 hours of recovery, NK activity did not differ significantly from baseline levels. Cortisol levels at 5 minutes post-exercise were negatively correlated with NK activity at 1.5 hours of recovery ( $r = -0.62$ ,  $P = 0.05$ , 50:1 E:T ratio:  $r = -0.66$ ,  $P = 0.04$ , 25:1 E:T ratio). Further research is needed to elucidate the effect these changes have on host immunosurveillance and immunoresponsiveness *in vivo*.

**24. Berk, L.S., S.A. Tan, D.C. Nieman, and  
W.C. Eby:**

Stress from maximal exercise modifies T-helper and T-suppressor lymphocyte subpopulations and their ratio in man.

In: *Exercise Physiology: Current Selected Research*, vol. 3, edited by C.O. Dotson. New York: AMS Press, Inc., 1988. p. 1-11.

**Authors' abstract**

Acute changes in peripheral blood lymphocyte subpopulations Leu-3a (T-helper) and Leu-2a (T-suppressor) and their ratio (H/S) were studied in athletes and non-athletes in response to stress from maximal exercise. Eleven male athletes (mean age 43) and 9 male non-athletes (mean age 44) were exercised to maximal physical exertion utilizing the Balke stress treadmill protocol. Subjective maximal physical exertion was determined by a 10-point Scale Rating of Perceived Exertion. Peak  $\dot{V}O_2$  for athletes and non athletes were  $54.2 \pm 1.8$  and  $33.3 \pm 1.1$  ( $\bar{X} \pm SE$ ) ml/kg/min respectively, ( $P < 0.05$ ). Blood samples were obtained from an indwelling intravenous (i.v.) catheter 10 minutes before the exercise period and 15 minutes after the stress of maximal exercise. The percentages of T-helper and T-suppressor lymphocytes of total T-lymphocytes were enumerated using a direct fluorescence-conjugated monoclonal antibody procedure; the H/S were determined from these data. T-helper lymphocytes were decreased and T-suppressor lymphocytes increased in both groups after the stress from maximal exercise ( $P < 0.05$ ). A one sample t-test on the ratio of paired pre- to post-exercise H/S for athletes and non-athletes showed a statistically

significant decrease ( $P < 0.03$ ;  $P < 0.01$ , respectively). These data suggest that stress resulting from maximal exercise in both conditioned and unconditioned individuals may have a propensity to modulate immune surveillance by decreasing the H/S.

**25. Berk, L.S., S.A. Tan, D.C. Nieman, and W.C. Eby:**

The suppressive effect of stress from acute exhaustive exercise on T-lymphocyte helper/suppressor cell ratio in athletes and non-athletes.  
*Medicine and Science in Sports and Exercise* 17:492, 1985.

**Authors' abstract**

We studied the effects of acute exhaustive exercise on T-lymphocyte helper and suppressor cells, and their ratio (H/S). Twelve male subjects, seven athletes (mean age 43) and five non-athletes (mean age 42) were placed on a treadmill (Balke protocol with continuous metabolic monitoring), and exercised to exhaustion. Peak  $\dot{V}O_2$  ( $\bar{X} \pm SD$ ) for athletes and non-athletes were  $55.0 \pm 6.8$  and  $32.7 \pm 3.1$  ml/kg/min, respectively. Helper and suppressor cells, and the H/S were determined from blood samples taken 10 minutes pre and 15 minutes post exercise using a direct immunofluorescence procedure with monoclonal Leu-2a and Leu-3a antibodies (Becton Dickinson). Pre-exercise helper cells were  $62.7 \pm 9.8\%$  of total lymphocytes, and post-exercise were  $57.4 \pm 10.3\%$ . The decrease was significant ( $p < 0.05$ ) using a paired t-test ( $t = 2.59$ ). Suppressor cells were  $37.5 \pm 10\%$  pre and  $42.6 \pm 10.3\%$  post-exercise. The increase was significant ( $t = 2.53$ ;  $p < 0.05$ ). Before exercise, the H/S of athletes ( $2.17 \pm 0.86$ ) was not significantly different ( $t = 1.67$ ;  $p > 0.05$ ) from that of non-athletes ( $1.43 \pm 0.54$ ). After exercise the H/S difference between athletes ( $1.8 \pm 1.12$ ) and non-athletes ( $1.21 \pm 0.58$ ) was not significant ( $t = 1.06$ ;  $p > 0.05$ ). These findings suggest that acute exhaustive exercise has significant effect on the H/S, which may modify the immune response. Further research is needed to assess not only other immunological parameters that are suppressed with excess exercise, but also those enhanced with optimal exercise.

**26. Bieger, W.P., M. Weiss, G. Michel, and H. Weicker:**

Exercise-induced monocytosis and modulation of monocyte function.  
*International Journal of Sports Medicine* 1:30-36, 1980.

**Authors' abstract**

Twenty male volunteers underwent short-term treadmill exercise with stepwise acceleration until exhaustion. Blood samples were analyzed before, during, and after exercise. The number of circulating white blood cells increased (81.6% increase) resulting in lymphocytosis (131%) and a minor granulocytosis (56.5%). The most pronounced increase was observed with B-lymphocytes (225%) followed by T-lymphocytes (110%) and monocytes (87%). The serum levels of immunoreactive insulin (56%) increased, glucagon (42%), cortisol (62%), and most pronounced, growth hormone (2340 %) rose substantially. The metabolic activity of circulating monocytes was slightly enhanced after exhaustive exercise: 2-deoxyglucose uptake increased by 12.5%, glucose oxidation via the pentose phosphate shunt rose by 13.5%, whereas the anaerobic formation of lactate remained unchanged. Incubation of resting monocytes with insulin alone had the same but more pronounced effects on glucose metabolism (34% and 36% increase, respectively). Under the same conditions, dexamethasone decreased glucose oxidation and the anaerobic glycolysis but had no influence on glucose uptake. Exercise as well as insulin and dexamethasone slightly depressed the phagocytic activity of monocytes when incubated with opsonized zymosan particles. In conclusion exercise provokes changes in the number and function of circulating monocytes, which correspond to those induced by insulin (and dexamethasone) in resting cells. The increase in circulating hormone concentrations and the enhanced insulin sensitivity of monocytes after exercise may therefore be responsible for some of these changes. It is not known to which extent the results are influenced by the changes in the circulating mononuclear cell pool.

**27. Bierman, H.R., K.H. Kelly, F.L. Cordes, N.L. Petrakis, H. Kass, and E.L. Shpil:**

The influence of respiratory movements upon the circulating leukocytes.  
*Blood* 7:533-544, 1952.

**Synopsis**

**Purpose** To study changes in number and differential count of the leukocytes in circulating venous and arterial blood with regard to respiratory movements.

### Methods

1. The leukocyte content of venous and arterial blood of 17 subjects was studied frequently during respirations and the Valsalva and Muller maneuvers.

2. The venous and arterial samples were drawn simultaneously and were obtained by direct puncture from freely flowing peripheral venous or arterial blood, or by catheterization from the right ventricle, pulmonary artery, hepatic vein, left ventricle, or aorta.

### Results

1. During the Valsalva maneuver the arterial leukocyte count decreased markedly with relatively little alteration in the simultaneous venous counts; upon release of the forced expiration both counts promptly regained the control level.

2. During the Muller maneuver increases in both arterial and venous leukocyte counts occurred in one subject, while no significant effect was observed in venous samples in a second subject.

3. During inspiration the arterial leukocyte count fell and the simultaneous venous count rose with reciprocal changes upon expiration. These changes occurred whether the initial counts were elevated, normal, or leukopenic.

4. The changes in leukocyte number of both arterial and venous blood during respiratory movements were not due to hemoconcentration or hemodilution and suggest a significant tidal ebb and flow of leukocytes into and from the pulmonary circulation.

### Conclusions

1. Whether the leukocytes are merely mechanically sequestered temporarily in the pulmonary capillaries during inspiration and released during expiration is not clear.

2. The greater changes in the polymorphonuclear cells may reflect their greater number or their greater tendency to stick to surfaces or capillary endothelium with slowed circulation as occurs in the pulmonary vascular bed during the Valsalva maneuver.

3. The possible role of some chemical factor is not excluded.

## 28. Blatt, W.F., and J. Kerkay:

The effect of repeated heat and cold exposure on serum protein composition in man.  
*Canadian Journal of Physiology and Pharmacology*  
45 : 571-575, 1967.

### Authors' abstract

Total protein, serum protein, and lipoprotein electrophoretic distribution and hematocrit values were determined in two groups of men during acclimatization to 6 weeks of cold and 11 days of heat, respectively. After 3 weeks of cold exposure total serum protein and albumin content decreased, while the globulin fractions increased; thus, the calculated albumin/globulin ratio was significantly depressed. During the last 2 weeks, these parameters gradually returned to control values. Overall, the protein changes during heat acclimatization were minimal, although the globulins decreased slightly, yielding a small increase in the albumin/globulin ratio. The hematocrit levels were significantly lowered during both environmental exposures, whereas the lipoprotein distribution remained essentially unchanged.

## 29. Bosenberg, A.T., J.G. Brock-Utne, S.L. Gaffin, M.T.B. Wells, and G.T.W. Blake:

Strenuous exercise causes systemic endotoxemia.  
*Journal of Applied Physiology* 65:106-108, 1988.

### Authors' abstract

Eighteen triathletes were studied before and immediately after competing in an ultradistance triathlon. Their mean plasma lipopolysaccharide (LPS) concentrations increased from 0.081 to 0.294 ng/ml ( $P < 0.001$ ), and their mean plasma anti-LPS immunoglobulin G (IgG) concentrations decreased from 67.63 to 38.99  $\mu\text{g/ml}$  ( $P < 0.001$ ). Both pretriathlon plasma LPS and anti-LPS IgG levels were directly related to the intensity of training ( $P < 0.02$  and  $P < 0.01$ , respectively). It is possible that training-induced stress led to some leakage of LPS into the circulation, which, in turn, resulted in self-immunization against LPS. The effects on athletic performance in relation to exercise-induced changes in plasma LPS and anti-LPS IgG levels require further investigation.

**30. Brahmi, Z., J.E. Thomas, M. Park,**

**M. Park, and I.R.G. Dowdeswell:**

The effect of acute exercise on natural killer-cell activity of trained and sedentary human subjects.

*Journal of Clinical Immunology* 5:321-328, 1985.

**Authors' abstract**

The effect of acute exercise on natural killer (NK) activity and on the distribution of phenotypic characteristics of peripheral blood lymphocytes was examined. Trained and sedentary individuals underwent a standard progressive exercise test on a cycle ergometer using an incremental work load of 15 W (90 kpm), increased every minute. Each subject was encouraged to exercise to exhaustion, and total ventilation and mixed expired O<sub>2</sub> and CO<sub>2</sub> were measured every 30 seconds. All subjects reached the "anaerobic" threshold as judged by the deflection of ventilation at a work load near VO<sub>2</sub>max. NK activity against K562 reached maximum levels immediately after exercise, dropped to a low point 120 minutes later, then slowly came back to pre-exercise levels within 20 hours. No significant differences were observed between the trained and the sedentary groups. Furthermore, immediately after exercise the proportion of OKT-3+ and OKT-4+ cells was reduced by 29.8 ± 3.6 and 33.6 ± 5.4%, respectively; the percentage Leu-7+ and Leu-11a+ cells was increased by 53.9 ± 1.7 and 57.3 ± 2.9% respectively. The percentage of OKT-8+ cells was not significantly altered. When the percentage binding of effector to target cells was examined, it was highest at 0 minutes post-exercise (19 ± 6.2%) and lowest at 120 minutes post-exercise (7 ± 3.9%), but the absolute number of NK cells remained unchanged. The source of serum used in the lytic assay had no effect on NK activity, as fetal calf serum and autologous sera drawn at different time intervals during exercise gave similar results. Epinephrine suppressed and interferon enhanced the NK activity of all cells tested, which indicates that during and after exercise NK cells did not go through a refractory stage. Our results show that, contrary to other lymphocyte subpopulations, NK cells are resistant to the depletive and modulatory effects of acute exercise and the increase in NK activity is not due to an increase in the absolute number of NK cells.

**31. Brodde O.-E., A. Daul, and N. O'Hara:**

β-Adrenoceptor changes in human lymphocytes, induced by dynamic exercise.

*Naunyn-Schmiedeberg's Archives of Pharmacology* 325:190-192, 1984.

**Authors' abstract**

In 10 healthy volunteers the effects of acute increases in concentrations of catecholamines in plasma induced by dynamic exercise (on a bicycle for 15 minutes at 80% of maximum heart rate) on lymphocyte β-adrenoceptor density (determined by ( ± ) 125iodocyanopindolol binding) and responsiveness (determined by cyclic AMP responses to 10 μmol/l isoprenaline) were investigated. Immediately after exercise plasma catecholamines were increased about 4-fold; concomitantly receptor density and cyclic AMP production increased 55% and 65%, respectively. One hour after exercise β-adrenoceptor density and plasma catecholamines had reached values which were not significantly different from pre-exercise values, while cyclic AMP production was significantly diminished. It is concluded that acute increases in concentrations of catecholamines in plasma may increase β-adrenoceptor density and responsiveness in human lymphocytes.

**32. Burman, K.D., E.W. Ferguson,**

**Y.-Y. Djuh, L. Wartofsky, and**

**K. Latham:**

Beta receptors in peripheral mononuclear cells increase acutely during exercise.

*Acta Endocrinologica* 109:563-568, 1985.

**Authors' abstract**

Five healthy adult well trained men (averaging 49 miles running per week) were exercised to exhaustion on a treadmill. Plasma epinephrine increased from 168 ± 37 pg/ml prior to exercise to 633 ± 345 pg/ml immediately after exercise (P < 0.025) in the two respective periods. Beta receptor density increased from 53 ± 18 fmol/mg protein before exercise, to 223 ± 63 fmol/mg (P < 0.05) protein immediately after exercise, and then decreased to 83 ± 27 fmol/mg protein one hour later (P < 0.05 compared to post-exercise). The mean Kd value prior to exercise of 1.5 × 10<sup>-11</sup>M was unchanged statistically throughout the study.

Following correction for haemodilution, serum total and free T<sub>4</sub> and T<sub>3</sub> concentrations were also unchanged during exercise, although reverse T<sub>3</sub> levels did increase from 39 ± 4 to 45 ± 0 ng/dl (P < 0.05). These findings suggest that: 1) plasma epinephrine, norepinephrine and beta receptor density, but not Kd, increase acutely during



exercise, and 2) total and free T<sub>4</sub> and T<sub>3</sub> after correction for haemodilution, do not change during acute exercise. Our data indicate that acute exercise represents an unusual condition during which 'down regulation' is not observed, but, rather, there appear to be parallel alterations in beta receptor density and plasma catecholamine levels.

**33. Buschmann, H. and M. Baumann:**

Alterations of cellular immune response during intensive training of event horses.  
*Journal of Veterinary Medicine* 38:90-94, 1991.

**Authors' abstract**

During strenuous exercise of horses that are prepared for international Three-Day Events a significant decrease in the *in vitro* killing rate of phagocytosed yeast cells by the blood granulocytes has been observed. Other immunological parameters, such as the phorbolmyristate dependent chemiluminescence in granulocytes and the mitogenic stimulation of blood lymphocytes, remained unchanged.

**34. Busse, W.W., C.L. Anderson, P.G. Hanson, and J.D. Folts:**

The effect of exercise on the granulocyte response to isoproterenol in the trained athlete and unconditioned individual.

*Journal of Allergy and Clinical Immunology* 65:358-364, 1980.

**Authors' abstract**

Many factors will influence the tissue response to catecholamine stimulation. Isolated human granulocytes (PMNs) release the lysosomal enzyme  $\beta$ -glucuronidase following incubation with complement-activated zymosan particles. Isoproterenol, histamine, and prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) inhibit this PMN release of  $\beta$ -glucuronidase. The effect of exercise on this *in vitro* granulocyte response was studied in two groups; highly conditioned marathon runners (n = 6) and unconditioned subjects (n = 7). A 13 km run did not produce leukocytes in the highly trained marathon runners and the granulocyte response to isoproterenol was unchanged in cells obtained immediately following the run. In contrast, the seven unconditioned subjects exercised to a maximal response on the treadmill. Following exercise there was an increase in plasma catecholamines, a significant leukocytosis, and granulocytes from the immediate post-exercise period responded less well to isoproterenol.

**35. Butler, J., J.G. Kelly, K. O'Malley, and F. Pidgeon:**

$\beta$ -Adrenoreceptor adaptation to acute exercise.  
*Journal of Physiology* (London) 344:113-117, 1983.

**Authors' abstract**

1. The effects of strenuous exercise on lymphocyte  $\beta$ -adrenoreceptor density and responsiveness in nine men were biphasic.
2. There was an initial increase in receptor density, seen immediately after exercise, with a subsequent decline to below pre-exercise values.
3. In parallel, maximum isoprenaline-stimulated cyclic AMP production by lymphocytes was greatly increased at the end of exercise and decreased thereafter.
4. The increases seen at the end of exercise may be of functional significance and may represent a response of the tissue to the demands placed upon it. After a time, however, a desensitization process takes over, possibly with a protective role.

**36. Butler, J., M. O'Brien, K. O'Malley, and J.G. Kelly:**

Relationship of  $\beta$ -adrenoreceptor density to fitness in athletes.  
*Nature* 298:60-62, 1982.

**Synopsis**

**Purpose** To measure lymphocyte  $\beta$ -adrenoreceptor density in athletes before and after an extensive training program.

**Methods**

1. Sixteen male swimmers (age 14-24 years) of varying fitness embarked on a 2-month intensive training program.
2. No subject was taking drugs.
3. At 10:30 a.m. a 30 ml venous blood sample was drawn from each subject, at 11:00 a.m. each subject underwent submaximal exercise on a Monarch cycle ergometer and fitness levels were assessed.
4. Seven subjects satisfactorily completed their training schedule and were reassessed.

**Results**

1. Training increased max  $\dot{V}O_2$  in every case, from a mean of  $48.7 \pm 4.5$  ml/kg to a mean of  $58.1 \pm 4.1$  ml/kg ( $P < 0.05$ , student's t-test for paired data).

2. After training, lymphocyte  $\beta$ -adrenoreceptor density in the seven subjects decreased from a mean of  $1,074 \pm 152$  receptors per cell to a mean of  $458 \pm 78$  receptors per cell ( $P < 0.05$ ).

3. Receptor density decreased in all but one subject (his changed from 547 to 554 sites per cell).

4. Subjects showing the greatest increase in fitness tended to show the greatest fall in lymphocyte  $\beta$ -adrenoreceptor density.

5. There was a significant linear correlation between change in receptor density and change in max  $\dot{V}O_2$ .

#### Conclusions

1. Physical training can reduce  $\beta$ -adrenoreceptor density and this reduction is proportional to changes in fitness.

2. The decreased sympathetic nervous system responsiveness seen in athletes is probably due to decreased  $\beta$ -adrenoreceptor density resulting from chronic exposure to high concentrations of catecholamines.

### 37. Calabrese, J.R., M.A. Kling, and

P.W. Gold:

Alterations in immunocompetence during stress, bereavement, and depression: Focus on neuroendocrine regulation.

*American Journal of Psychiatry* 144:1123-1134, 1987.

#### Authors' abstract

There is now clear evidence that stress, bereavement, and depression can compromise specific components of the immunological apparatus. The first part of this paper gives an overview of fundamental immunology and is followed by a review of the patterns, possible causes, and potential clinical implications of abnormal immunoregulation. After a discussion of the immunomodulating properties of glucocorticoids, the authors conclude with an overview of the many factors that mediate the complex interdependence between immunologic function, the brain, and neuroendocrine regulation.

### 38. Calabrese, L.H.:

Exercise, immunity, cancer, and infection.

In: *Exercise, Fitness, and Health*, edited by

C. Bouchard, R.J. Shephard, T. Stephens, J.R. Sutton, and B.D. McPherson. Champaign, IL: Human Kinetics Publishers, 1990. p. 567-579.

#### Author's synopsis

Could the overall decreased incidence of all forms of cancer observed in physically active individuals, the significantly decreased incidence of cancer of the colon in physically active men, and the decreased incidence of cancer of the reproductive organs in collegiate women athletes be explained on the basis of enhanced immunosurveillance? Data that support such a hypothesis clearly are lacking at present, and several lines of reasoning seem to suggest that this is not the most plausible explanation:

- Neoplasms that are observed most frequently in immunosuppressed individuals are those of lymphoreticular origin, and it would be suspected that individuals with heightened immunologic surveillance would show a significantly decreased incidence of these tumors when compared to those previously described.

- If heightened immunologic surveillance contributes to a decreased incidence of cancer, there should be observed a decrease in all forms of cancer, not only those of the colon and breast.

- These malignancies least frequently observed in physically active individuals (i.e., colon in men and reproductive organs in women) are not those frequently associated with immunosuppression.

- Although immunologic adaptation to exercise and training appears to be a real phenomenon, those adaptations thus far described are inconsistent, frequently of small magnitude, and not associated with clear clinical implications.

Alternatively, in light of the general paucity of data published on this subject, there are arguments supporting the role for enhanced immunologic surveillance against malignancy induced by exercise and training:

- Studies performed thus far investigating immunologic adaptation as a function of exercise and training have been limited in number and largely flawed in design and have not utilized the most relative and sophisticated immunologic techniques to assess host defenses against malignancy.

- Observations identifying a significantly decreased incidence of only certain forms of tumors may reflect the fact that immune surveillance is not equally important for all types of cancer.

- The expected decrease in lymphoreticular neoplasms has not been observed in physically active individuals. It is possible that these cancers arise only in immunosuppressed individuals as the result of a complication of immunosuppression (i.e., lack of immunoregulation of lymphocyte proliferation) as opposed to lack of immunosurveillance.

- The protective effect of physical activity on immune surveillance may be at an extremely low threshold of physical activity, as described by Paffenbarger et al. (34), and of extremely small magnitude, limiting its detection in currently published studies.

Thus, in light of the fact that the data thus far reviewed are largely preliminary and controversial, it appears premature to discount totally the role of immunologic adaptation from exercise and training in altering host defenses to infections for malignancies.

### 39. Calabrese, L.H., S.M. Kleiner, B.P. Barna, C.I. Skibinski, D.T. Kirkendall, R.G. Lahita, and J.A. Lombardo:

The effects of anabolic steroids and strength training on the human immune response.

*Medicine and Science in Sports and Exercise* 21:386-392, 1989.

#### Authors' abstract

The immune response was assessed in 13 competitive bodybuilders self administering anabolic-androgenic steroids and ten competitive bodybuilders not administering these drugs. Laboratory assessment included the number and relative distribution of T-cells, T-helper/inducer cells, T-cytotoxic/suppressor cells, activated T-cells, lymphocyte transformation to the mitogens pokeweed mitogen (PWM), phytohemagglutinin (PHA), Concanavalin-A (CON-A), *Staphylococcus aureus* Cowan strain I (SAC), serum immunoglobulins, and natural killer (NK) activity. There were no significant differences in T-cell subsets among steroid users and non-users, but lymphocyte transformation studies revealed that the anabolic-androgenic steroid-using group had enhanced proliferative ability to the  $\beta$ -cell mitogen, SAC, in comparison to non-bodybuilding controls. NK activity was significantly ( $P < 0.05$ ) augmented in the anabolic-androgenic steroid users but not in the non-using bodybuilders. Serum immunoglobulin levels, in particular IgA, were significantly ( $P < 0.017$ ) lower in the steroid-using group. Four of 13 steroid users and three of eight non-steroid-using bodybuilders had detectable antinuclear antibodies. These studies indicate that 1) anabolic-

androgenic steroid use as practiced by contemporary athletes is a potent modulator of immune responsiveness, and 2) autoantibodies are prevalent in strength-trained men even in the absence of anabolic steroid use.

### 40. Calabrese, L.H., S.M. Kleiner, and J.A. Lombardo:

The effect of anabolic steroids on the immune response in male body builders.

*Medicine and Science in Sports and Exercise* 19:S52, 1987.

#### Authors' abstract

The widespread use of anabolic steroids (AS) in athletics has necessitated careful study of their biologic effects in order to predict potential toxicity. Though male sex hormones are known perturbors of immune responsiveness in animals, there are no data on their effect in man in doses commonly used in athletics. We have examined a variety of immunologic parameters in male body builders on AS ( $n = 13$ ) as well as two groups of controls, body builders not on AS ( $n = 10$ ) and non-body builders. Absolute and relative percentages of lymphocytes, T-cells, T-helper/inducer cells, T-cytotoxic/suppressor cells and activated T-cells did not differ among the groups. Lymphocyte proliferation to the mitogens Con-A, PWM, PHA and *Staff. aureus* Cowan strain-I showed a trend toward higher responses in the AS users. Immunoglobulins were significantly lower in AS users vs. controls for IgG, IgM and IgA ( $P < 0.04$ ). Based upon these preliminary studies we conclude: 1) AS use is associated with suppressed humoral immunity as evidenced by lower immunoglobulin levels, 2) AS users tend to have higher lymphocyte proliferative activity *in vitro*, and 3) the significance of these findings are of unknown clinical significance at present.

### 41. Cameron, K.:

Haematological profiles and polyclonal lymphocyte function in continuous and intermittent exercise.

*Masters Thesis: University of Western Australia, 1987. 160 p.*

#### Author's abstract

There is some anecdotal evidence that trained athletes tend to experience a relatively high incidence of minor infections. The effects of exercise on the immune system are still not well established, particularly as in the limited research which has been conducted, the exercise stresses imposed on the subjects have often been poorly controlled. The effects of 3 exercise protocols (aerobic, glycolytic, phosphate) on haematological profiles and on

polyclonal lymphocyte function *in vitro* were determined in 10 conditioned ( $\text{VO}_2\text{max } 64 \pm 2.5 \text{ ml/kg/min}$ ) male team sport players. Total circulating leucocyte numbers were significantly raised after each of the aerobic ( $P < 0.01$ ), glycolytic ( $P < 0.001$ ) and phosphate ( $P < 0.001$ ) protocols. The percentage increase in leucocyte number was positively correlated with heart rate at the end of exercise ( $P < 0.001$ ) and with the venous lactate after exercise ( $P < 0.001$ ). The *in vitro* responses of the leucocytes to the polyclonal T-cell stimulators phytohaemagglutinin (PHA) and concanavalin A (ConA) were not significantly suppressed when the three exercise protocols were treated separately. The responses to the  $\beta$ -cell mitogen pokeweed mitogen (PWM) was significantly suppressed after the aerobic protocol ( $P < 0.05$ ). There were no differences between the effects of the 3 different exercise protocols on the changes to lymphocyte function *in vitro*, therefore the data for the three protocols were combined and referred to as nonspecific exercise. Nonspecific exercise resulted in significant suppression of the H-DNA synthetic response of lymphocytes to PHA and to PWM, but not to ConA. The use of indomethacin in the leucocyte cultures established that the observed effect on *in vitro* lymphocyte transformation was unlikely to be due to increased local prostaglandin production after exercise. In a second trial, a leucocyte sample from each subject was cultured with serum which had been collected before and after exercise. Serum which had been collected after exercise did not significantly inhibit the mitogen response compared to pre-exercise serum. In the third trial, 6 subjects exercised according to the same three exercise protocols as used in trial 1. The T4/T8 ratios of each subject's peripheral blood were determined before and after exercise in conjunction with H-DNA synthesis of circulating lymphocytes. The T4/T8 ratios were significantly lower after exercise than before exercise in the glycolytic ( $P < 0.01$ ) and phosphate ( $P < 0.01$ ) protocols although not after the aerobic protocol ( $P < 0.1$ ). Although the responses of lymphocytes to mitogens were not on average affected by exercise, the percent increase in lymphocyte radioactive DNA synthesis was correlated with both pre-exercise T4/T8 ratios. The results of this study suggest that a temporary, generalized suppression of lymphocyte activity may occur post-exercise. The mechanisms of the effects of exercise on *in vitro* lymphocyte function remain unknown.

**42. Camus, G., D. Sondag, J. Maggipinto, J. Pincemail, A.F. Plumier, F. Feron, A. Juchmes-Ferir, J. Duchateau, M. Lamy, G. Deby-Dupont, and C. Deby:**

Mobilisation des leucocytes lors de l'exercice dynamique sous-maximum.  
*Archives Internationales de Physiologie, de Biochimie et de Biophysique* 99:419-423, 1991.

#### Authors' abstract

Increase of blood leucocytes induced by a dynamic exercise has been studied in 10 adult male subjects (age:  $22 \pm 2$  years; body weight:  $73 \pm 10 \text{ kg}$ ;  $\text{VO}_2\text{max}$ :  $54 \pm 8 \text{ ml O}_2/\text{kg}\cdot\text{min}$ ). The exercise consisted of a 20 minute test on a cycle ergometer at a work rate eliciting a total energy expenditure roughly equal to 80% of the maximal aerobic power (80%  $\text{VO}_2\text{max}$ ). During exercise the absolute number of circulating leucocytes (n Leu) increased significantly toward a maximal value reached in most cases at the end of exercise. The maximal values of n Leu—expressed as a percentage of n Leu measured at rest—in the different blood leucocyte types (monocytes: n Mono; granulocytes: n GR; natural killer cells: n NK) and lymphocyte subsets (lymphocytes: n LY; lymphocytes T: n T; lymphocytes B: n B; lymphocytes T helper: n T4; lymphocytes T suppressor: n T8) were as follows: n Mono: 240%; n GR: 170%; n NK: 490%; n LY: 220%; n T: 200%; n B: 190%; n T4: 140%; n T8: 190%. With the exception of n GR, n Leu decreased during recovery at a rate depending on the leucocyte type. The n T4/n T8 ratio, equal to 1 at rest was reduced by about 40% during exercise. This ratio rose after exercise and reached a value equal to that measured at rest after 20 minutes recovery. In agreement with Ferry (1989), we concluded that exercise is accompanied by a selective mobilization of the different leucocyte types. The magnitude of this phenomenon and the kinetics of n Leu recuperation depend on cell types.

**43. Cannon, J. and C. Dinarello:**

Interleukin-1 activity in human plasma.  
*Federation Proceedings* 43:462, 1984.

#### Authors' abstract

Interleukin-1 (IL-1) seems to be identical to endogenous pyrogen (EP), leukocyte endogenous mediator (LEM) and lymphocyte activation factor (LAF) which mediate, respectively, fever, trace metal metabolism and lymphocyte proliferation. While LEM (J. Inf Dis. 126:77) and EP (Science 220:617) activities have been detected in human plasma, LAF activity has not. Whole human plasma inhibits mitogen induced proliferation of murine

thymocytes making detection of circulating LAF impossible by this technique. An analogous system using monocyte depleted human lymphocytes responded inconsistently to whole plasma. However, plasma fractions separated by gel filtration were effectively assayed by the standard murine system. Suppressor eluted at > 50 kilodaltons (kd) while stimulatory factors consistently eluted at 11-13, 2-4 and ca. 1 kd when plasma from febrile (n = 3) or healthy subjects after exercise (n = 3) was tested. Although the material was diluted at least 6-fold, fractions from febrile patients doubled the mitogen response and post-exercise fractions produced a 30-60% increase. The 11-13 kd material was inactivated by 30-min at 70°C; the 2-4 kd material was not. These data indicate a useful assay system for circulating IL-1. They also support previous observations regarding exercise as a stimulus for IL-1 production and that IL-1 may break down to smaller active fragments (Br.J.Path. 61:534).

**44. Cannon, J.G., W.J. Evans, V.A. Hughes, C.N. Meredith, and C.A. Dinarello:**

Physiological mechanisms contributing to increased interleukin-1 secretion.  
*Journal of Applied Physiology* 61:1869-1874, 1986.

**Authors' abstract**

Interleukin 1 (IL-1) is a monocyte-derived polypeptide that mediates many host defense adaptations to environmental and infectious stresses. This investigation was intended to characterize further IL-1 activity found in human plasma following exercise and to identify physiological initiators of IL-1 secretion. IL-1 activity was measured by the ability of plasma fractions to stimulate lymphocyte proliferation. This activity appeared in plasma several hours after exercise on a cycle ergometer (1 h at 60% of aerobic capacity, n = 8 subjects) and was neutralized with a specific antiserum to human IL-1. The hypothesis that IL-1 release from monocytes was initiated by phagocytosis of material from cells damaged by exercise was tested. The increase in IL-1 activity did not correlate significantly ( $r = 0.55$ ) with creatine kinase activity, a marker for release of intracellular proteins into the circulation, and IL-1 secretion by monocytes was not stimulated by incubation with red blood cell lysates *in vitro*. Thus the stimulus for IL-1 secretion did not appear to be related to a scavenging function of monocytes. The possibility that IL-1 secretion may be mediated by stress hormones associated with exercise was examined. IL-1 secretion by monocytes was increased up to  $48 \pm 18\%$  ( $P < 0.01$ ) by addition of physiological concentrations of epinephrine *in vitro*. Low concentrations of hydrocortisone (1 ng/ml) also augmented IL-1 secretion by  $58 \pm 20\%$ . Higher concentrations in the

physiological range had no effect, and combinations of epinephrine and hydrocortisone suppressed IL-1 secretion. These results indicate that IL-1 activity can be altered *in vivo* by the physiological stress of exercise and *in vitro* by hormones associated with stress, but epinephrine and hydrocortisone do not appear to mediate the elevation of IL-1 activity in exercise.

**45. Cannon, J.G., R.A. Fielding, M.A. Fiatarone, S.F. Orencole, C.A. Dinarello, and W.J. Evans:**

Increased interleukin 1 $\beta$  in human skeletal muscle after exercise.  
*American Journal of Physiology* 257:R451-R455, 1989.

**Authors' Abstract**

Interleukin 1 $\beta$  (IL-1 $\beta$ ) is a protein released from blood monocytes and related cells in response to infectious or inflammatory stimuli. Although IL-1 $\beta$  is elevated in the circulation for only a few hours after an acute inflammatory challenge or exercise, it has been proposed to mediate anabolic and catabolic processes that can last for several days. In this report, eccentric exercise was used as a noninfectious inflammatory stimulus. IL-1 $\beta$  was found in muscle tissue up to 5 days after exercise using specific immunohistochemical tissue staining. Increased IL-1 $\beta$  immunoreactivity was observed in muscle tissue from 4 human subjects who performed the exercise, but not in tissue obtained at the same time intervals from 2 subjects who did not exercise. Little immunohistochemical evidence of interleukin-1 $\alpha$  or tumor necrosis factor  $\alpha$  was observed before or after exercise. These results implicate IL-1 $\beta$  in the metabolic adaptations of muscle tissue, which occur in response to noninfectious stresses.

**46. Cannon, J.G. and M.J. Kluger:**

Endogenous pyrogen activity in human plasma after exercise.  
*Science* 220:617-619, 1983.

**Authors' abstract**

Plasma obtained from human subjects after exercise and injected intraperitoneally into rats elevated rat rectal temperature and depressed plasma iron and zinc concentrations. The pyrogenic component was heat-denaturable and had an apparent molecular weight of 14,000 daltons. Human mononuclear leukocytes obtained after exercise and incubated *in vitro* released a factor into the medium that also elevated body temperature in rats and reduced trace metal concentrations. These results suggest that endogenous pyrogen, a protein mediator of

fever and trace metal metabolism during infection, is released during exercise.

**47. Cannon, J.G., and M.J. Kluger:**

Exercise enhances survival rate in mice infected with *Salmonella typhimurium*.  
*Proceedings of the Society for Experimental Biology and Medicine* 175:518-521, 1984.

**Authors' abstract**

Mice voluntarily trained on exercise wheels for 16-18 days and were then infected with an approximate LD50 dose of *Salmonella typhimurium*. These trained mice exhibited a small, but statistically significant ( $P = 0.037$ ) increase in survival rate (34/77) compared to sedentary control mice (23/79) after 7 days.

**48. Carmack, M.A.:**

Exercise-induced modifications in immune responsiveness in rats.  
*Doctoral Dissertation*: University of Oregon, 1984.  
73 p.

**Author's abstract**

This study was undertaken to examine selected parameters of immune function following a period of chronic aerobic exercise. Fifteen Sprague-Dawley rats, divided evenly into three groups, were exercised for 32 weeks by swimming either 60 minutes (S-60 rats), 30 minutes (S-30 rats), or 0 minutes (S-0 rats) on a continuous schedule of two exercise days followed by one rest day. At the conclusion of the 32-week exercise program, serial blood sampling was commenced to evaluate absolute numbers of lymphocytes, *in vitro* mitogenic response of peripheral lymphocytes, and *in vivo* antibody response to inoculation with sheep red blood cells (SRBCs). The first blood samples (Day 0) were drawn immediately after each animal's final swim to permit detection of any acute effects. Subsequent samples were drawn on days 3, 11, 18, 25, and 32 following termination of exercise to assess persistence and recovery of any immune modifications. Whole blood mitogenic stimulation with concanavalin A was performed on samples drawn on each of Days 0, 3, 11, and 18. Analysis of the absolute numbers of lymphocytes in blood samples confirmed that the cultures contained equivalent concentrations of lymphocytes. A significant difference ( $P = .007$ ) among the groups in lymphocyte stimulation response was found only on Day 3. At this point, the stimulation index of the S-60 rats was significantly higher than that for the S-0 rats ( $P = .035$ ); titer differences between groups were not significant. The stimulation

index of the S-30 rats was intermediate between the S-60 rats and S-0 rats but was not significantly different from either. Comparison of the pooled S-60 and S-30 rats versus the S-0 rats was significant ( $P = .024$ ). The *in vivo* antibody response to inoculation with SRBCs (on Day 3) was evaluated by antibody hemagglutination assays of samples drawn on days 3, 11, 18, 25, and 32. Antibody titers were consistently highest for the S-60 rats, intermediate for the S-30 rats, and lowest for the S-0 rats. Thus, the ordering of antibody responsiveness among the three groups paralleled the ordering of mitogenic stimulation responsiveness on Day 3. However, antibody titer differences between groups were not significant.

**49. Carr, D.B., B.A. Bullen, G.S. Skrinar, M.A. Arnold, M. Rosenblatt, I.Z. Beitins, J.B. Martin, and J.W. McArthur:**

Physical conditioning facilitates the exercise-induced secretion of beta-endorphin and beta-lipotropin in women.  
*New England Journal of Medicine* 305:560-563, 1981.

**Synopsis**

**Purpose** To study opioid-peptide levels in normal non-athletic women (18-30) during exercise and to determine whether the chronic increase in energy output by sedentary persons undergoing physical conditioning affects their opioid-peptide responses to acute exercise.

**Methods**

1. The subjects were tested during the early follicular phase of their menstrual cycles over four successive months of physical training.
2. Exercise test sessions were done at the beginning, midpoint, and end of training.
3. The control group sat on an exercise bike for 1 hr. The exercise group pedaled up to 85% maximum pulse rate for 1 hr.
4. The control and exercise groups had 2 baseline blood samples drawn 15 min apart.
5. Blood samples were taken at 1 hr and at 30 min of recovery.
6. Blood samples were assayed for total  $\beta$ -endorphin,  $\beta$ -lipotropin, and cortisol.

**Results**

1. Acute rises in  $\beta$ -endorphin and  $\beta$ -lipotropin during exercise were greater in the second session than in the first.

2. The final cortisol level in each session rose significantly after one month of training, as well as in the first and last blood samples of any session.

3. Mean ACTH levels showed no change during the control session, rose 63% in the pre-training exercise test, and rose by 116% after two months of training.

#### Conclusions

1. There is a concomitant release of  $\beta$ -endorphin,  $\beta$ -lipotropin, and ACTH during training.

2. ACTH rises in untrained women in whom no cortisol rise is apparent during exercise.

3. Acute exercise causes a rise in  $\beta$ -EP and  $\beta$ -LPH, and exercise training augments this effect.

#### 50. Casper, H.:

Veränderungen des weissen Blutbildes nach dem 100 m-Lauf bei Frauen.  
*Zeitschrift für die Gesamte Physikalisch Therapie*  
30:5-14, 1925.

#### Synopsis

After a 100-m run, the behavior of the white cells was examined in 33 women, all in good physical condition. Leukocytosis occurred: lymphocytes were responsible for the largest portion, and neutrophils for the smallest; eosinophils and monocytes were in the middle range. There was a small increase in platelets.

#### 51. Chastain, L.L.:

Time relations of changes in the leucocyte count due to strenuous muscular activity.

*Masters Thesis*: Vanderbilt University, 1935. 66 p.

#### Author's summary

1. Leucocyte count of a given individual in either the condition of random activity or physiologic rest may be used as a norm following increases produced in the total leucocyte count by strenuous muscular activity.

2. The range of random activity counts and resting counts is definitely increased during the afternoon hours over the range observed for these respective conditions in the early morning. This is due to the fact that the upper limit is elevated in afternoon counts while the low level is not elevated.

3. Similar to the effect of strenuous muscular activity upon the respiratory rate, heart rate and blood pressure, the effect upon the total leucocyte count may persist for a considerable period beyond the duration of the exercise.

4. The return of the elevated total leucocyte count toward lower initial levels following an increase in count produced by muscular activity of short duration is relatively rapid, but is dependent upon the severity of the exercise and the degree of leucocytosis thereby produced, and in no small measure on the lability of the vasomotor system for any given individual.

5. Repeated periods of exercise when properly spaced may produce repeated and equal increases in the leucocyte count where the exercise is constant for duration and severity.

6. The increase in the total leucocyte count produced by repetitions or exercise may be summed, provided the period elapsing between exercise periods is not sufficient for a complete return to the initial level of the leucocyte count. The total leucocyte count produced by the summing or increases may be as great as the maximal physiologic leucocyte count for a given type of exercise in a given individual, provided there is sufficient repetition of the exercise, which must however be relatively severe.

7. The rapidity with which the increase in circulating leucocytes takes place, and the similar rapid decline in the count, the striking fact that increases amounting to 35% can be induced at will and as frequently as desired by simple repetitions of the bout of exercise is sufficient evidence that a fraction of the cells already existing in the vascular bed is brought into the count with each repetition and that they are not created de novo or derived exclusively from leucocyte forming loci in bone marrow. The rise and decline of the count is apparently due to the promptness or vasomotor responses which results in redistribution and alteration or sequestration in the capillary bed.

#### 52. Christensen, R.D. and H.R. Hill:

Exercise-induced changes in the blood concentration of leukocyte populations in teenage athletes.  
*American Journal of Pediatric Hematology/Oncology*  
9:140-142, 1987.

#### Authors' abstract

Neutrophilia following exercise is well described in adults and children. However, the effects of exercise on less concentrated leukocyte populations, such as circulating colony forming unit-granulocyte macrophage (CFU-GM), CFU-granulocyte, erythrocyte, megakaryocyte, macrophage (CFU-GEMM), and the various lymphocyte subsets, is not clear. To obtain this information, members of a high school track team were asked to run flights of stairs at their most rapid pace for

ten minutes. Prior to and 5 minutes following exercise, blood concentrations of various leukocyte populations were measured. As expected, the circulating neutrophil concentration increased following exercise (26% increase). However, the largest post-exercise increases were in eosinophils (139% increase) and lymphocytes (67% increase). The increase in blood lymphocytes was primarily due to an increase in total T-cells (52% increase) and T-suppressor cells (49% increase), with no significant elevation in T-helper cell or B-cell populations. The exercise did not induce an increase in the immune/total neutrophil ratio or in the number of circulating CFU-GM or CFU-GEMM.

### 53. Cohen, L.A., K. Choi, and C.-X. Wang:

Influence of dietary fat, caloric restriction, and voluntary exercise on *N*-nitrosomethylurea-induced mammary tumorigenesis in rats.  
*Cancer Research* 48:4276-4283, 1988.

#### Authors' abstract

The effect of dietary fat, energy restriction, and exercise on *N*-nitrosomethylurea (NMU:CAS:684-93-5)-induced mammary tumorigenesis in female F344 rats was investigated. Rats were fed the NIH-07 diet until *N*-nitrosomethylurea administration on Day 50 of age, when they were transferred to six treatment groups. Three sedentary groups were fed either high-fat (20%, w/w), medium-fat (10%), or low-fat (5%) diets *ad libitum* (HFAL, MFAL, LFAL, respectively); two sedentary groups were fed high fat and medium fat diets restricted to 75% of the food consumed by their *ad libitum* counterparts (HFR, MFR), and one group was fed a HFAL diet but allowed free access to an activity wheel (HFEX). Tumor yields among the three *ad libitum* sedentary groups were significantly greater in the HFAL and MFAL groups when compared to the LFAL group. Dietary restriction reduced tumor yields by more than 90% of *ad libitum* controls regardless of fat intake. Voluntary exercise reduced tumor yields and delayed time of tumor appearance in HFEX animals to levels similar to those found in LFAL animals. Animals with voluntary access to exercise wheels averaged between 1.03 and 2.85 miles/day, consumed more food (+18%), and exhibited greater weight gain (+13%) than their sedentary counterparts. Restricted animals exhibited significantly decreased body weight gains (~15% compared to their *ad libitum* counterparts, but no differences in weight gain were detected among the HFAL, MFAL, and LFAL groups, despite widely varying amounts of fat intake. Body composition studies indicated that body fat content was not influenced by the quantity of fat consumed in the diet, but was significantly reduced

by caloric restriction (~20 to 26%) and exercise (~20%). While the precise mechanisms underlying the tumor-promoting effects of HFAL diets and the antipromoting effects of energy restriction and exercise remain to be elucidated, available evidence suggests that these effects are not due to alterations in energy homeostasis *per se*, but may instead be exerted indirectly, and perhaps independently via endocrine, paracrine, or neurohormonal mechanisms.

### 54. Colacino, D.L. and B. Balke:

Tumor reduction in continuous and interval endurance trained mice.  
*Medicine and Science in Sports and Exercise* 7:90, 1975.

#### Authors' abstract

To further test the application of exercise in the prevention of cancer in man, 3 parameters were investigated: (1) interval training was compared to continuous-endurance training (1972) Colacino and Balke, (2) carcinogens were compared using 7, 12 DMBA and a known initiator, BPL, and (3) non pre-trained mice were compared to pre-trained and control sedentary mice. Weekly tumor counts were compared between mice exercised daily on a treadmill, to those of controls who had been housed in cages permitting them only limited activity. Except for the group of 15 mice which constituted a non-pre-trained interval exercise group, the skin tumors were initiated after the exercised animals had received ten weeks of training. 7, 12 DMBA and BPL were used to initiate the tumor growth of the respective groups and croton oil was applied weekly to promote it. Thirty-two weeks of daily running on a treadmill of either continuous or interval exercise endurance training regimen, revealed the number of tumors of the controls exceeded those of the exercised mice. The final mean was 13.4 tumors/control as opposed to 7.2 tumors/exercised mouse. More important, 98% of the control mice had tumors whereas 24% of the exercised mice were tumor-free compared to 8% in the non-pre-trained interval exercise BPL group and 5% in the control (sedentary) BPL mice. The interval DMBA group was 31% tumor-free compared to 0% tumor-free in the DMBA control mice.



**55. Colt, E.W.D., S.L. Wardlaw, and**

**A.G. Frantz:**

The effect of running on plasma  $\beta$ -endorphin.  
*Life Sciences* 28:1637-1640, 1981.

**Authors' abstract**

Plasma  $\beta$ -endorphin immunoactivity was measured by RIA in 26 trained long distance runners on 35 occasions before and after running. Mean total  $\beta$ -endorphin immunoactivity increased from  $11.8 \pm 1.8$  (SEM) to  $17.6 \pm 3.1$  pg/ml in 20 runners after an easy run ( $P = 0.067$ ), and from  $8.2 \pm 1.03$  to  $28.0 \pm 6.3$  pg/ml in 15 runners after a strenuous run ( $P = 0.008$ ). Total  $\beta$ -endorphin immunoactivity in the plasma extracts of 7 runners before and after the strenuous run was further characterized by Sephadex G-50 chromatography in order to separate  $\beta$ -endorphin from crossreacting  $\beta$ -lipotropin ( $\beta$ -LPH). A rise in  $\beta$ -endorphin and  $\beta$ -LPH concentrations after running was noted in 5 out of 7 runners.

**56. Crist, D.M., L.T. Mackinnon,**

**R.F. Thompson, H.A. Atterbom, and  
P.A. Egan:**

Physical exercise increases natural cellular-mediated tumor cytotoxicity in elderly women.  
*Gerontology* 35:66-71, 1989.

**Authors' abstract**

The influence of acute treadmill exercise on natural killer (NK) cell tumor cytotoxicity *in vitro* was studied in elderly women after participation in a program of physical exercise training (PET) ( $n = 7$ ) or after participation in a paralleling non-exercise control (NEC) condition ( $n = 7$ ). The two study groups were equated ( $P > 0.05$ ) according to age, percent total body fat, functional status as measured by multi-inventory ranking, and exercise capacity. After the experimental period, the PET subjects had a greater basal level of NK activity than the NEC subjects (PET 38.2 percent specific lysis, %SL, vs. NEC 28.8 %SL;  $P < 0.05$ ). Both groups experienced an increase in NK activity after acute treadmill exercise (PET 38.2-57.4 %SL,  $P < 0.01$ ; NEC 28.8-37.8 %SL,  $P < 0.05$ ), but the increase in the PET subjects was significantly ( $P < 0.05$ ) greater than that observed in the NEC subjects. We conclude that natural cellular-mediated tumor cytotoxicity is increased in response to acute and long-term PET in elderly women.

**57. Cross, B.B.:**

The effect of aerobic conditioning on antibody production in Balb/C mice.  
*Doctoral Dissertation: University of Maryland,*  
1985. 68 p.

**Author's abstract**

Seven female Balb/C mice were studied to ascertain the effect of a sixteen week treadmill running program on antibody production. Nine age matched females served as controls. The running program was considered of sufficient intensity to elicit aerobic benefits based on the findings of a significantly ( $P < 0.05$ ) higher heart weight to body weight ratio and SDH activity in the exercised mice. On weeks twelve and fifteen, all mice were given interperitoneal injections of 100  $\mu$ g dinitrophenolated bovine serum albumin (DNP-BSA) to elicit an antibody response. Six and nine days after each injection serum was assayed for antibodies against DNP-BSA by radioimmunoassay. Analysis of variance for repeated measures revealed no significant ( $P > 0.05$ ) difference between the exercise and control group with regard to either their primary or secondary response to DNP-BSA. In contrast to what has been previously reported, these data suggest that the amount of antibody produced by Balb/C mice in response to a challenge with DNP-BSA is not affected by aerobic conditioning.

**58. Cundell, D., J. Danks, M.J. Phillips, and  
R.J. Davies:**

Effect of exercise on isoprenaline-induced lymphocyte cAMP production in atopic asthmatics and atopic and non-atopic, non-asthmatic subjects.  
*Clinical Allergy* 14:433-442, 1984.

**Authors' abstract**

The effect of exercise on isoprenaline-induced cyclic adenosine monophosphate (cAMP) production was studied in peripheral-blood lymphocytes obtained from ten patients with atopic asthma, seven subjects who were atopic but did not have asthma and eight non-atopic, non-asthmatic control subjects. The asthma in the atopic subjects was mild only requiring intermittent treatment with inhaled  $\beta$  adrenoreceptor agonists, none of which were taken in the 48 hours prior to the study. Exercise consisted of a standardized 6-min run on a treadmill sufficient to raise the subjects pulse rate to  $>160$  bpm and respiratory function was measured before and at 5, 10, 15, 20, 30, and 60 minutes after the test. Blood samples were taken 5 minutes before and at 10 and 60 minutes after exercise, lymphocytes were separated by density gradient centrifugation and cAMP measured by a competitive radioimmunoassay. Exercise led to a significant decrease

(27%) in the forced expiratory volume in 1 second (FEV<sub>1</sub>) in the ten atopic asthmatic subjects but no change (<3%) in the non-atopic and atopic non-asthmatics. There was no significant difference in the unstimulated cAMP levels before exercise in the three groups, but stimulation with isoprenaline caused a significantly greater rise in cAMP in the non-atopic, non-asthmatic subjects when compared to both the atopic asthmatics and the atopic subjects without asthma. Exercise led to a significant elevation of cAMP in all three groups of subjects, but the same differences between the groups remained. These results suggest that there are differences in lymphocyte  $\beta$  receptor function not between patients who are asthmatic or non-asthmatic but between individuals who are atopic as opposed to non-atopic.

**59. Daniels, W.L., D.S. Sharp, J.E. Wright, J.A. Vogel, G. Friman, W.R. Beisel, and J.J. Knapik:**

Effects of virus infection on physical performance in man.

*Military Medicine* 150: 8-14, 1985.

**Authors' abstract**

Nine subjects (seven experimentals, two controls) were studied in order to measure physical performance before, during, and after an experimentally induced episode of sandfly fever. During the fever, experimental subjects displayed decreases in measures of isometric muscle strength and isokinetic knee extensor strength at 36°/second. Three out of the seven subjects were unable to complete a submaximal exercise walk during the fever. Rectal temperature was elevated throughout the walk, but no other physiological parameter was significantly altered. After fever, submaximal exercise performance and muscle strength were similar to the prefever values. Our results indicate that a mild viral infection will diminish isometric strength during fever, as well as cause a marked effect upon the ability and/or willingness of some individuals to perform exercise at gradually increasing intensity.

**60. Davidson, R.J.L., J.D. Robertson, G. Galea, and R.J. Maughan:**

Hematological changes associated with marathon running.

*International Journal of Sports Medicine* 8:19-25, 1987.

**Authors' abstract**

Coulter profiles with differential white cell counts, serum ferritin, and haptoglobin levels were determined in

venous blood samples obtained from 90 males (M) and 25 females (F) immediately before and after completion of a competitive marathon (42.2 km) race. In an additional 20 male runners, the same measurements were performed serially during the 24 hours following their completion of the race. In the pre-race samples from 90 M and 25 F, hypoferritinemia was present in 4/22 M and 1 F found to be mildly anemic. Neutropenia was detected in 4 M and 3 F and mild thrombocytopenia in 2 M. Haptoglobin levels were normal in all the female runners but reduced (<0.3 g/l) in 6 M. All post-race samples (88 M and 25 F) were characterized by a reactive neutrophilia and thrombocytosis including those with pre-race neutrophilia or thrombocytopenia. An unexpected and incompletely explained sex difference in packed cell volume (PCV) response was observed. In males, the mean PCV increased from  $0.425 \pm 0.021$  to  $0.444 \pm 0.028$  ( $P < 0.0001$ ) whereas in females it decreased from  $0.437 \pm 0.029$  to  $0.423 \pm 0.036$  ( $P < 0.05$ ). In the post-race samples, anahaptoglobinemia was found in 13/88 M and 4/25 F. In the 20 male runners studied serially for 24 hours after the race, the major changes involved a progressive increase in mean plasma volume ( $17.4\% \pm 12.2\%$  at 24 hours) compared with the pre-race value, a progressive and significant increase in MCH and MCHC probably indicating a loss in red cell water and the gradual reversion of the reactive neutrophilia and thrombocytosis to basal levels.

**61. Davis, M.A., Z.V. Kendrick, and A.M. Paolone:**

Measurement of antibody response to influenza virus vaccine in aerobically trained mice.

*Medicine and Science in Sports and Exercise* 18:S9, 1986.

**Authors' abstract**

The antibody responses of four groups of Swiss Webster mice, ten per group, to the influenza virus vaccine were studied. Two groups were exercised on a treadmill for ten weeks. One of these groups was vaccinated with the virus vaccine, and the other was not. The two remaining groups were unexercised, with one being vaccinated with the virus and the other not vaccinated. The work intensity of the exercised groups was gradually increased until the mice were able to run for one hour per day, five days per week at .58 mph. All mice were bled from the tail three days before training began and again two days after training ended. The two groups receiving the vaccine were injected intraperitoneally with 0.1 ml of vaccine, containing eight microgram hemagglutination units of influenza virus, seventeen days before the training ceased. The succinic dehydrogenase activity was measured in the

gastrocnemius muscle of two mice from each group to ensure that a training effect existed in the mice. All sera collected from the mice were tested for degree of antibody response to the vaccine using an enzyme-linked immunoabsorbent assay (ELISA). There was no significant difference between the antibody responses of the untrained and trained mice to the vaccine. It can be concluded that exercise did not enhance the mice's ability to mount an antibody response to a virus vaccine.

- 62. Debavelaere, C., J. de Blic, C. Bodemer, D. Teillac, J. Paupe, and P. Scheinmann:**  
Syndrome d'anaphylaxie induite par l'exercice.  
*Archives Francaises de Pediatrie* 46:281-283, 1989.

#### Authors' abstract

The authors report the case of a 12-year-old boy with exercise-induced anaphylaxis. Angioedema was the main symptom and was accentuated by ingestion of an orange prior to exercise. Exercise-induced anaphylaxis is due to mast cell degranulation that is triggered by exercise alone or, less commonly, by the combination of a sensitizing food and exercise. The symptoms of exercise-induced anaphylaxis may be moderate or severe, with laryngeal dyspnea and shock. Prevention is based on avoidance of the offending food before exercise and a reduction of the intensity (and even the suppression) of exertion.

- 63. DeBlasi, A., A.S. Maisel, R.D. Feldman, M.G. Ziegler, M. Fratelli, M. DiLallo, D.A. Smith, C.Y.C. Lai, and H.J. Motulsky:**

*In vivo* regulation of  $\beta$ -adrenergic receptors on human mononuclear leukocytes: Assessment of receptor number, location, and function after posture change, exercise, and isoproterenol infusion.  
*Journal of Clinical Endocrinology and Metabolism* 63:847-853, 1986.

#### Authors' abstract

We studied the regulation of  $\beta$ -adrenergic receptors in human mononuclear leukocytes (MNL). Total receptor number was determined as specific binding of 4 C of [ $^3$ H]dihydroalprenolol or [ $^{125}$ I]iodopindolol, and redistributed receptors were defined as those binding sites to which the hydrophilic antagonist CGP-12177 did not have access. Receptor function was assessed as cAMP accumulation stimulated by isoproterenol. In *in vitro* experiments, high concentrations of isoproterenol desensitized receptor function and promoted redistribution of about 80% of the receptors away from the cell surface. However, three *in vivo* protocols (upright posture

for 3 hours, moderate exercise, and infusion of isoproterenol for 30 minutes) redistributed few  $\beta$ -adrenergic receptors on MNL. The 30 minute isoproterenol infusion did not alter later cAMP accumulation, but posture change and exercise increased isoproterenol-stimulated cAMP accumulation in intact MNL. Infusion of isoproterenol for 120 minutes redistributed  $9 \pm 2\%$  ( $\pm$  SEM) of the receptors and decreased isoproterenol-stimulated cAMP accumulation by  $19 \pm 6\%$ . Isoproterenol-stimulated adenylate cyclase activity in membranes isolated from MNL previously was found to be decreased with upright posture, and we confirmed these findings in assays that did not include exogenous GTP, but instead relied upon guanine nucleotides retained in the membrane preparation. However, when excess GTP was included, isoproterenol-stimulated adenylate cyclase activity in MNL membranes was not altered by posture change. We conclude that substantial receptor redistribution of  $\beta$ -receptors on MNL does not readily occur in physiological situations.

- 64. De la Fuente, M., M.I. Martin, and E. Ortega:**

Changes in the phagocytic function of peritoneal macrophages from old mice after strenuous physical exercise.

*Comparative Immunology, Microbiology and Infectious Diseases* 13:189-198, 1990.

#### Authors' abstract

The effect of acute physical exercise (swimming until exhaustion) on the phagocytic function of peritoneal macrophages from old adult BALB/c mice ( $55 \pm 5$  weeks old) was studied. Adherence capacity of macrophages to substrate, spontaneous mobility, and chemotaxis as well as digestion capacity measured by nitroblue tetrazolium (NBT) reduction in presence of ingested material (latex beads), were not modified with exercise. Adherence to nylon fiber, opsonization and ingestion of *Candida albicans* (either spontaneous or in presence of serum), ingestion of latex particles as well as nitroblue tetrazolium (NBT) reduction in absence of ingested material (oxidative metabolism measure) were increased with respect to controls with statistically significant differences ( $P < 0.001$ ) in peritoneal macrophages after the exercise.

**65. De Lanne, R., J.R. Barnes, and**

**L. Brouha:**

Hematological changes during muscular activity and recovery.

*Journal of Applied Physiology* 15:31-36, 1960.

**Authors' abstract**

Hematological changes were studied in men and women during exercise and recovery under three environmental conditions. An erythrocytosis due to hemoconcentration was observed which was not followed by hemodilution and was not accompanied by the destruction or generation of red cells. Hemoconcentration was influenced by exercise, but not by thermal stress, in spite of greater water losses in warm environments. Sex differences at rest were found for red and white cells, but the pattern of the reactions to exercise was similar for both sexes. Leucocytosis resulted from exercise and heat exposure, with a greater effect of exercise in the females. This is due to increased capillary circulation, hemoconcentration and lymphatic pressure, but not to the stimulation of leucopoietic centers. Changes in the systemic circulation followed by an increase of lymph flow explain the lymphocytosis. Granulocytosis occurs later, persists longer, and may be related to the concentration of circulating corticosteroid hormones.

**66. De Rosa, G. and N.R. Suarez:**

Effect of exercise on tumor growth and body composition of the host.

*Federation Proceedings* 29:1118, 1980.

**Authors' abstract**

Tumor growth and changes in body composition were studied in 70 day old rats bearing a transplanted Morris 7800 hepatoma and receiving measured amounts of a semipurified 24% casein diet. The animals were exercised in motorized training cages either from the day of tumor inoculation for 21 days, or trained for 30 days prior to tumor inoculation and then exercised for 21 days. In all groups larger tumor masses developed at larger food intakes. The weights of the neoplasms harvested from exercising rats however were always smaller than those harvested from non-exercising ones; even smaller tumors developed in rats trained for 30 days prior to tumor inoculation. The tumor growth response to food intake obtained in trained animals was smaller than that obtained in exercising animals, which was in turn smaller than the growth response obtained in non-trained non-exercised rats. The body growth rates of the experimental animals was not significantly affected by either training or exercise nor by the presence of a developing tumor. Greater lean mass deposition occurred in exercised

animals relative to the controls and training resulted in even larger deposition of lean tissue. On the basis of these results it is proposed that physical exercise inhibits tumor growth by enhancing the competition for nutrients between host and tumor.

**67. Deuster, P.A., G.P. Chrousos,**

**A. Luger, J.E. DeBolt, L.L. Bernier,**

**U.H. Trostmann, S.B. Kyle,**

**L.C. Montgomery, and D.L. Loriaux:**

Hormonal and metabolic responses of untrained, moderately trained, and highly trained men to three exercise intensities.

*Metabolism* 38:141-148, 1989.

**Authors' abstract**

Untrained, moderately trained (runners, 15 to 25 mi/wk), and highly trained (runners, >45 mi/wk) men participated in graded treadmill exercise at 50%, 70%, and 90% of their maximal oxygen consumption to quantify the relation between the intensity of exercise and sympathetic nervous system and metabolic responses. Sympathetic system activation was noted at all intensities tested and was proportional to the relative exercise intensity. The magnitudes of the norepinephrine (NE) and epinephrine (E) responses were similar in all three groups of men at each relative exercise intensity and correlated with the magnitudes of change in levels of circulating plasma adrenocorticotropin hormone, cortisol, lactate (La), phosphate (Pi), and glucose (Gl). The magnitude of change in concentrations of La, Pi, and Gl were also similar for the three groups at each relative exercise intensity. In contrast, a lower degree of sympathetic system activation in response to a given absolute workload was noted in the moderately and highly trained men as compared to that of the untrained men. Sympathetic and metabolic responses to exercise are similar under conditions of comparable relative intensities, regardless of conditioning level. The sympathetic-adrenal medullary system is more sensitive to exercise than the hypothalamic-pituitary-adrenal axis. For a given absolute workload, the degree of activation is significantly lower in trained individuals.

**68. Deuster, P.A., A.M. Curiale, M.L. Cowan, and F.D. Finkelman:**

Exercise-induced changes in populations of peripheral blood mononuclear cells.  
*Medicine and Science in Sports and Exercise* 20:276-280, 1988.

**Authors' abstract**

The effects of maximal treadmill exercise on changes in the expression and distribution of peripheral blood B-lymphocytes, T-lymphocytes, and natural killer cells (NK) were examined in 20 healthy men with a mean age of  $32.0 \pm 1.3$  years. The percentage and absolute number of peripheral blood mononuclear cells that reacted with specific monoclonal antibodies which bind to B-cells (anti-Leu-12 and anti-human-immunoglobulin D-delta chain specific), T-cells (OKT3), and NK cells (anti-Leu-11 and anti-Leu-7) were enumerated by a fluorescence-activated cell sorter in samples obtained before (Pre), immediately after (Post), and 1 hour after a bout of exercise to exhaustion. In contrast to earlier studies, the results of this study indicate that maximal exertion effects a decrease in the percentage, but no change in the absolute number of peripheral blood B-cells (Pre:  $0.21 \pm 0.01$ ; Post:  $0.31 \pm 0.02$  cells  $\times 10^{-6}/\text{ml}$ ). In addition, a small, transient increase in the number of peripheral blood cells reacting with surface markers associated with T-lymphocytes (Pre:  $1.15 \pm 0.09$ ; Post:  $2.05 \pm 0.19$  cells  $\times 10^{-6}/\text{ml}$ ) and a striking, transient increase in lymphocytes having NK phenotype activity (Pre:  $0.34 \pm 0.03$ ; Post:  $1.51 \pm 0.19$  cells  $\times 10^{-6}/\text{ml}$ ) were noted. All of the pre-exercise values were re-established 1 hour after exercise. Whether the mobilization of cells with surface markers associated with NK activity in response to maximal exertion serves any physiologic function during periods of physical stress remains to be determined.

**69. Deuster, P.A., S.D. Morrison, and R.A. Ahrens:**

Endurance exercise modifies cachexia of tumor growth in rats.  
*Medicine and Science in Sports and Exercise* 17:385-392, 1985.

**Authors' abstract**

Food intakes, body composition, skeletal muscle mass, muscle protein synthesis, and myofibrillar protein degradation were studied in normal, food restricted (FR), and Walker 256 tumor-bearing (TB) male Sprague-Dawley rats which were exercised (E) or maintained in a sedentary state. Exercise was enforced 3 times per week

for 100 min/session at 20 m/min. on a 13% incline for 7 weeks. Tumors were transplanted 3 weeks after beginning the exercise program and were allowed to grow for 29 days. Food restriction was initiated during the last two weeks of tumor growth. Food intakes and body lipid stores were reduced in all E groups, whereas body nitrogen was reduced only in the TB animals. All E animals had significantly higher gastrocnemius muscle/body weight ratios than their sedentary counterparts, with the greatest ratio noted for the TBE animals. Muscle protein synthesis, measured by incorporation of [ $^3\text{H}$ ]tyrosine into gastrocnemius muscle, was significantly depressed in both FR and TB animals. Muscle protein breakdown, estimated by urinary 3-methylhistidine excretion, was significantly elevated in TB animals and slightly increased in FR animals. The results suggest that tumor presence significantly alters protein turnover to a greater extent than elicited by food restriction alone. Additionally, although exercise may have initially protected the animal by retarding tumor growth and muscle mass depletion, in the end, the energy costs of exercise accelerated the catabolic state.

**70. Dorian, B. and P.E. Garfinkel:**

Stress, immunity and illness—a review.  
*Psychological Medicine* 17:393-407, 1987.

**Authors' synopsis**

Psychological factors have long been thought to play a contributing role in either the predisposition, onset or course of various physical illnesses. Recently, rapid advances in immunology have created interest in the interaction between psychosocial factors, behavior and the immune system. This paper reviews some of the models proposed to explain the relationship between psychological variables and physical illness and presents evidence for a contribution of psychological factors to certain illnesses in which abnormalities in immunologic state are thought to be important. From a somewhat different perspective, animal studies have demonstrated complex effects of stress on disease susceptibility. Recent human studies have demonstrated consistent immunologic changes in people undergoing acute naturally occurring psychological stress such as bereavement or an important examination. In humans, the effects of chronic stress may be different from acute stress, corresponding to the findings in animals. Abnormalities in immunologic functioning and physical illness are reviewed for different psychiatric disorders—depression, anorexia nervosa and schizophrenia: depression is the only disorder which consistently demonstrated immunologic changes. Possible mechanisms for the stress/immune-change relationship are suggested.

### 71. Dörner, H., D. Heinhold, and W. Hilmer:

Exercise-induced leukocytosis—its dependence on physical capability.

*International Journal of Sports Medicine* 8:152, 1987.

#### Authors' abstract

Both the total leukocytes and the leukocyte differential picture were studied on 216 endurance-trained volunteers (37 females and 179 males) at the age between 12 and 71 years. Blood samples were taken before and immediately after exhaustive exercise on an electrodynamically braked bicycle ergometer in a sitting position. The subjects have been divided in eight groups regarding their physical capability in the exercise test ranging from 1.5 W/kg BW to 5.0 W/kg BW. Under resting conditions there was a significant depression of total leukocytes in the groups with high ergometric work capacity (4.5 W/kg avg. = 6163; 5.0 W/kg avg. = 5650) compared to the groups with low work capacity (1.5 W/kg avg. = 6967; 2.0 W/kg avg. = 7653). The lower total phenomenon has been well described and is thought to be due to endurance training. Immediately after exercise the total leukocytes were found to be increased in all groups. The increase was significantly higher in the two best groups with 4607(4.5 W/kg) leuko/nl and 4332 (5.0 W/kg) compared to the two poorest groups with 3101 (1.5 W/kg) and 3554 (2.0 W/kg) on the average. In the leukocyte differential picture there were significant changes in the neutrophil granulocytes and the lymphocytes after exercise. In the groups with high physical capacity the exercise-induced leukocytosis is mostly composed of granulocytes, in the groups with lower physical capability mostly of increased lymphocytes. By forming a quotient of the two cell fragments as  $Q = \text{granulocytes/lymphocytes}$  the changes in the leukocyte differentiated picture can be made visible in a simplified form. The difference between  $Q_2$  (after exercise) and  $Q_1$  (before exercise) shows continuously increasing values from  $-0.88$  in the group with 1.5 W/kg to  $+0.68$  in the group with 5.0 W/kg. The changes in both quantity and quality of the exercise-induced leukocytosis are caused by increasing plasma catecholamines and catecholamine receptors on the neutrophil granulocytes, which were found to be increased in endurance-trained subjects. The results show a dependence of the exercise-induced leukocytosis on the ergometric work capacity.

### 72. Douglas, D.J. and P.G. Hanson:

Upper respiratory infections in the conditioned athlete.

*Medicine and Science in Sports and Exercise* 10:55, 1978.

#### Authors' abstract

Sixty-one conditioned ( $\dot{V}O_2$  max  $55 \pm 76$  ml/kg/min) athletes (crew) and 126 unconditioned ( $\dot{V}O_2$  max  $30 \pm 54$  ml/kg/min) ROTC cadets were compared as to frequency and severity of specific URI symptoms using a validated symptom checklist during the last nine weeks of the 1977 fall semester. All were male students at a large midwestern university, 18-26 years old. Differences between the crew and the control group were evaluated using a t-test. The crew had more frequent and more severe symptoms than the control group ( $P < 0.05$ ) in the categories: stuffy nose, cough, malaise, laryngitis, aching joints and muscles, watery or burning eyes, and experienced nasal discharge and sore throat more severely but not more frequently than the controls. The controls had diarrhea more frequently and more severely than the crew. No significant differences were demonstrated between the groups in frequency or severity of sneezing, headaches, chilliness, shaking chills or fever. The crew saw a doctor and missed class more often than the cadets but the control group missed practice more frequently than the crew. These data indicate that the high exercise group in this study experienced selected URI symptoms more frequently and with greater severity than the control group.

### 73. Douglass, J.H.:

The effects of physical training on the immunological response in mice.

*Journal of Sports Medicine* 14:48-54, 1974.

#### Synopsis

**Purpose** To determine if physical training has an effect on the immunological response to diphtheria toxoid immunization.

#### Methods

1. Two groups of mice were immunized intraperitoneally with diphtheria toxoid.
2. One group was exercised daily for eleven weeks by swimming to near exhaustion in 30°C water, while the other group was not exercised but placed in a similar container with one half inch of water.
3. Pre-immune blood was drawn before and on the 7th and 14th postimmune days.

4. The mice were given a second immunization and blood was subsequently drawn 7 and 14 days later.
5. The FARR test was used for detection of antibody to 125 Iodine-labelled diphtheria toxin.

#### Results

1. No antibodies were detected in preimmune sera.
2. Only four mice in the unexercised group produced measurable amounts of antibody by the seventh day.
3. On the fourteenth day the average antibody produced in exercised mice was 1.32 LF units/ml, and 1.59 units/ml in the unexercised mice.
4. On the seventh day following secondary immunization the exercised mice produced an average of 34.9 LF units of antibody/ml serum, and the unexercised mice produced an average of 32.2 LF units antibody/ml serum.
5. On the fourteenth day after secondary immunization, the average antibody produced in exercised mice was 45.4 LF units/ml, with one mouse showing a decrease.
6. The unexercised mice had a decrease in average antibody produced to 32.2 and 29.3 LF units/ml of serum on days 28 and 35, respectively, following secondary immunization.

#### Conclusions

1. Exercise has an effect on the immunological response.
2. The antibody titer is enhanced in the exercised mice compared to that of the unexercised mice.

#### 74. Dufaux, B., K. Höffken, and W. Hollman:

Acute phase proteins and immune complexes during several days of severe physical exercise.

In: *Biochemistry of Exercise*, vol. 13, edited by H.G. Knutigen, J.A. Vogel, and J. Poortmans. Champaign, IL: Human Kinetics Publishers, 1983. p. 356-362.

#### Synopsis

**Purpose** To examine the serum concentration of C-reactive protein as a particularly sensitive indicator of an acute phase reaction and of circulating immune complexes before, during, and after 4 days of severe physical exercise.

#### Methods

1. Exercise load for 27 male subjects was determined by blood lactate levels of 4 mmol/L.
2. The subjects ran 25 km/day for 4 days. Blood samples were drawn on day 3 and 1 day after the race.

3. CRP, IgG, C4 and C3 were measured by immunoassay.
4. Circulating immune complexes were assessed by C1q binding and also by polyethylene glycol precipitation.

#### Results

1. Serum CRP was elevated and serum total protein was significantly decreased on day 3 of exercise and after the race when compared to pre-race values.
2. C3 and C4 were elevated on day 3 and after the race relative to serum total protein.
3. C1q binding assay was unchanged during and after the race relative to serum total protein.
4. IgG, C4, and C3 in PEG precipitate were elevated on day 3 compared with pre-race values.
5. C3 and C4 in PEG were slightly below pre-race levels after the race.

#### Conclusions

1. The increased content of IgG, C4, and C3 in the PEG precipitates reflects an elevation of 1C levels during the first few days of severe exercise with a return to normal or subnormal levels afterwards.
2. The absence of detectable 1C changes in the C1q binding assay may have been caused by the size and composition of the 1C involved.

#### 75. Dufaux, B., R. Müller, and W. Hollmann:

Assessment of circulating immune complexes by a solid-phase C1q-binding assay during the first hours and days after prolonged exercise.

*Clinica Chimica Acta* 145:313-317, 1985.

#### Authors' abstract

A sensitive and specific solid-phase C1q-binding assay using porcine C1q and microtitre plates as a solid phase, served to assess the immune complexes in serum during the first hours and days after a 3-hour running test.

Fourteen moderately trained male subjects participated in the race and covered  $36.3 \pm 3.7$  (mean  $\pm$  SD) km in 3 hours. Blood samples were drawn 1 day before, immediately before, immediately after, 1 and 3 hours after and 1, 2 and 4 days after the race. When corrected for the changes of serum total protein, the apparent immune complex concentrations were 1 and 3 hours after the race significantly higher ( $P < 0.001$  and  $P < 0.05$ , respectively) than the pre-exercise values. Two days after the race the values were significantly lower ( $P < 0.05$ ) than before the race. These findings provide evidence for the formation of immune complexes after severe physical exercise.

**76. Dufaux, B. and U. Order:**

Complement activation after prolonged exercise.

*Clinica Chimica Acta* 179:45-50, 1989.

**Authors' abstract**

The effects of a 2.5 hour running test on the concentrations of the complement cleavage products C3a, C4a and C5a in plasma were examined in 8 healthy young males. In all participants the C3a and C4a values were raised during (1 hour after the start) and immediately after exercise. C4a was also raised 1 and 3 hours after the race. These results provide evidence for complement activation after prolonged exercise.

**77. Dufaux, B. and U. Order:**

Plasma elastase-alpha-1-antitrypsin, neutrophin, tumor necrosis factor, and soluble interleukin-2 receptor after prolonged exercise.

*International Journal of Sports Medicine*  
10:434-438, 1989.

**Authors' abstract**

The effects of a 2.2 hour running test on the plasma concentrations of elastase-alpha-1-antitrypsin, neutrophin, tumor necrosis factor, and soluble interleukin-2 receptor were evaluated in eight healthy young male subjects. Neutrophin was measured by radioimmunoassay, elastase-alpha-1-antitrypsin, tumor necrosis factor, and soluble interleukin-2 receptor by enzyme immunoassay. The post-exercise values were corrected for plasma volume changes which were calculated from hematocrit and hemoglobin values. Compared with the concentrations before exercise, elastase-alpha-1-antitrypsin values were significantly increased during the run (1 hour after the start) ( $P < 0.01$ ) as well as during the first few hours after the end of the running test ( $P < 0.01$ ). A significant increase of tumor necrosis factor was observed 1 hour after the end and 1, 3 and 24 hours after the end of the running test, respectively ( $P < 0.01$ ), and soluble interleukin-2 receptor concentrations were significantly elevated 1 and 2 days after exercise ( $P < 0.01$ ). The increase of elastase-alpha-1-antitrypsin, neutrophin, tumor necrosis factor, and soluble interleukin-2 receptor supports the concept of a functional involvement of polymorphonuclear neutrophils and an activation of macrophages and T-lymphocytes after prolonged exercise.

**78. Dufaux, B., U. Order, H. Geyer, and**

**W. Hollmann:**

C-reactive protein serum concentrations in well-trained athletes.

*International Journal of Sports Medicine* 5:102-106, 1984.

**Authors' abstract**

Previously it had been shown that there is a sharp increase in C-reactive protein (CRP) serum concentration during the first few days after severe exercise. To evaluate the effect of physical training on the CRP levels, a sensitive enzyme immunoassay was developed and used to assess the basal CRP concentrations in 356 male and 103 female athletes, who trained at least four times per week in various disciplines, in 45 male and 40 female untrained controls, and in 35 elderly coronary patients. In male athletes the lowest CRP values were found in swimmers (median: 102 ng/ml,  $n = 59$ ), which were significantly lower ( $P < 0.001$ ) than those of male controls (median: 502 ng/ml,  $n = 45$ ). The CRP concentrations in rowers (median: 260 ng/ml,  $n = 108$ ) were also significantly lower ( $P < 0.01$ ) than in the control group. CRP levels in middle- and long-distance runners (median: 315 ng/ml,  $n = 53$ ), racing cyclists (median: 620 ng/ml,  $n = 111$ ), and soccer players (median: 660 ng/ml,  $n = 25$ ) did not differ significantly from those of the controls. In female athletes the lowest CRP concentrations were also found in swimmers (median: 110 ng/ml,  $n = 49$ ), which were significantly lower ( $P < 0.001$ ) than those of the female controls (median: 396 ng/ml,  $n = 40$ ). Female middle- and long-distance runners ( $n = 36$ ) and female rowers ( $n = 18$ ) had median CRP values of 250 and 285 ng/ml, respectively. These results suggest that training induces a suppressive effect upon CRP, responsible for the low serum levels in athletes (particularly swimmers) when compared to controls. CRP has a broad bacteriostatic action, hence low CRP levels in intensively training athletes could be implicated in an increased susceptibility for infections.

**79. Dufaux, B., U. Order, and W. Hollmann:**

Can physical exercise induce an effective fibrinolysis?

*Thrombosis Research* 36:37-43, 1984.

**Authors' abstract**

The study examined serum fibrin(ogen) degradation products (FDP/fdp) after short and prolonged exercise, before and after training, in young and elderly subjects. Six of 15 well-trained soccer players demonstrated an increase in FDP/fdp after a short graded maximal treadmill test. In 12 elderly subjects short maximal



exercise produced no increase of FDP/fdp. However, in most of these subjects an exhaustive work load was not reached. Three of 16 moderately trained young subjects exhibited a small FDP/fdp increase after 45 minutes of submaximal exercise and in 3 of 10 participants an elevation of FDP/fdp was found after a 3-hour running test. Immediately after the race there was a significant ( $P < 0.001$ ) increase of fragment D, measured by an enzyme immunoassay. During a second 3 hour race after an 8 week physical training program, the post-exercise FDP/fdp and fragment D increase was slightly enhanced. Plasma fibrinogen was significantly ( $P < 0.05$ ) elevated on the fourth day after the 3 hour race but not after the training program. In conclusion, intense and/or prolonged physical exercise caused only a modest increase of FDP/fdp. Physical training seems only minimally to affect this response. It is speculated that in the trained subject, daily exercise-induced fibrinolytic activation might be more relevant to the risk of thrombotic or atherosclerotic disease than a higher absolute resting or post-exercise fibrinolytic level compared with the untrained.

#### 80. Dufaux, B., U. Order, and H. Liesen:

Effect of a short maximal physical exercise on coagulation, fibrinolysis, and complement system.  
*International Journal of Sports Medicine*  
12:S38-S42, 1991.

##### Authors' abstract

In 11 healthy young subjects, the plasma concentrations of the thrombin-antithrombin III complex, fibrinopeptide A, tissue-plasminogen activator, complement fragments C3a and C4a, and histamine were measured before and after a graded maximal bicycle exercise test. The analyses were carried out 30 minutes before and immediately before exercise, immediately after exercise, and 30 and 60 minutes later. All post-exercise values were corrected for plasma volume changes, which were calculated from hematocrit and hemoglobin values. Immediately post-exercise, thrombin-antithrombin III, tissue-plasminogen activator, complement fragments C3a and C4a, and histamine were all significantly elevated ( $P < 0.01$ ), compared with the pre-exercise values; 30 and 60 minutes later the values normalized and significant differences from the pre-exercise values could no longer be measured. Fibrinopeptide A did not change significantly after exercise. The present results provide evidence for a simultaneous activation of coagulation, fibrinolysis, and complement system as well as for release of histamine after a short maximal exercise.

#### 81. Dunér, H. and B. Pernow:

Histamine and leukocytes in blood during muscular work in man.  
*Scandinavian Journal of Clinical and Laboratory Investigation* 10:394-396, 1958.

##### Synopsis

**Purpose** To determine change in blood histamine content during muscular work in humans..

##### Methods

1. 15 healthy persons aged 20 to 40 years exercised for 18-24 min on a bicycle ergometer; the women between 600 and 800 kpm per minute and the men between 900 and 1200 kpm per min.
2. A polythene catheter was inserted into a brachial artery and blood samples were taken before, and immediately before termination of the work at the maximal load.
3. White cell and differential counts were made.
4. In 10 of the subjects, 15 ml of blood were taken each time for measurement of histamine content. In 5 of the subjects, 25 ml of blood were taken and centrifuged for measurement of histamine content in plasma and blood cells separately.

##### Results

1. The histamine content of arterial whole blood before muscular work averaged  $4.2 \pm 0.7 \mu\text{g}$  per 100 ml of blood, and rose to  $6.7 \pm 0.7 \mu\text{g}$  per 100 ml of blood during maximal exertion ( $P < 0.001$ ); while white cell count averaged  $5,700 \pm 620$  and  $8,800 \pm 860$ , respectively ( $P < 0.001$ ).

2. White cell differential count showed no significant change.

3. In centrifuged blood there was a significant increase of the histamine content in both blood cells and serum.

##### Conclusions

1. It is uncertain whether the increase of histamine content in the serum is due to a diffusion of histamine from the increased leukocytes.
2. During muscular work histamine content increases in both serum and blood cells.

**82. Eberhardt, A.:**

Wplyw stresu emocjonalno-wysilkowego na odpornosc serologiczna organizmu. (Influence of emotional-exertion stress on serological resistance of the organism).

*Wychowanie Fizyczne Sport* 2:171-174, 1973.

**Author's abstract**

Great physical effort acts as a strong stress stimulus, it mobilizes the adaptation mechanisms of the organism. According to the theory of stress, a period of intensive physical work may correspond to a period of "preparation" characterized by a high activity of the pituitary-adrenal system and an enhanced secretion of transmitters of the nervous system. Emotional stimuli accompanying physical work additionally stimulate the nervous system, this being particularly visible in the activity of the vegetative system. Changes occur in catecholamines, serotonin and histamine secretion. Excessive physical effort not only affects the mechanisms of homeostasis, but causes unfavorable changes in tissue and cell metabolism. The following disturbances were noted: increased excretion of seromucoid and alpha-glycoproteins in urine, marked differences in the cytoplasmic enzymes, particularly in the blood cells, morphological and cytochemical changes in the tissues, disorders in the fibrinolytic activity of serum and urine, and disturbance of the acid-base balance.

**83. Eberhardt, A.:**

Effect of motor activity on some immunological mechanisms of nonspecific resistance of the body.  
I. Effect of physical effort of medium load.

*Acta Physiologica Polonica* 21:558-565, 1970.

**Author's abstract**

Experiments were performed on 19 human subjects. The first, a ten-person group, carried out a physical effort of medium load on Krogh's cycloergometer for 20 minutes, with a load of 700 kgm per min. The second, a nine-person group, attended a two-week skiing camp (860 m above sea level). The daily energy expenditure of subjects amounted to 3699 Kcal. The following parameters were determined: phagocytic index of leukocytes, effect of mercaptoethanol on the phagocytic activity, properdin level, complement titre, mean opsonin titre, content of IgG, IgA, and IgM immunoglobulins, titre of specific agglutinins, and hematocrit index. It was found that a single physical effort increased the level of phagocytic index, amount of properdin, and of IgM immunoglobulins content, while the titre of complement dropped. The content of IgG and IgA immunoglobulins and the opsonin titre did not vary. The ski training in the mountain climate

increased the phagocytic activity level, properdin content, and the amount of IgM immunoglobulins, while the opsonin and complement titre rose. The content of IgG and IgA immunoglobulins underwent no changes.

**84. Eberhardt, A.:**

Influence of motor activity on some serologic mechanisms of nonspecific immunity of the organism. II. Effect of strenuous physical effort.  
*Acta Physiologica Polonica* 22:185-194, 1971.

**Author's abstract**

Experiments were carried out on 17 human individuals. The first group was subjected to work on Krogh's bicycloergometer for 20 minutes (load of 1300 kgm per minute). The second group, composed of weight-lifters, attended a two week training camp (daily energy expenditures amounted to 5850 Kcal). The following indexes were studied: phagocytic index, effect of mercaptoethanol on phagocytosis, properdin level, complement titre, mean opsonins titre, amount of immunoglobulins IgG, IgA and IgM, specific agglutinins titre as well as the hematocrit. It was found that a single physical effort reduced the phagocytic index, and brought about a drop of the opsonins titre, did not change the properdin level or the amount of IgG, IgA and IgM immunoglobulins but increased the complement titre. During athletes' prolonged physical training the complement level, the phagocytic activity of leukocytes as well as the opsonin titre remained unchanged. Mercaptoethanol exerted no influence on the drop of phagocytosis after strenuous exercise. A marked relationship was found between the degree of adaptation to physical effort and changes of the immunity factors.

**85. Eberhardt, A. and S. Jasser:**

The influence of physical exercise and chronic starvation on serum levels of properdin and proteins in rats.

*Epidemiological Review* 21:278-284, 1967.

**Synopsis**

**Purpose** To investigate the influence of moderate physical exercise on properdin levels in underfed rats, and the influence of restricted diet on serum levels of properdin and proteins.

**Methods**

1. After determination of optimal dose of diet fodder, the rats were divided into three groups: Group I: 20 rats received a diet of 0.1g/1g body weight per 24 hours covering all caloric and vitamin requirements.

Group II: 10 rats received a diet covering 50% of caloric requirements with normal vitamin and mineral amounts for 4 months. Group III: 30 rats received a diet covering 20% of caloric requirements with normal vitamin and mineral amounts for 1.5 months.

2. Ten rats of each group I and II were ran on a treadmill for 18 min/day.

3. Blood was drawn from the tail vein before and after exercise and at the beginning of each experiment.

4. Properdin, total protein, and fractions were assayed.

#### Results

1. In group II, no significant differences in properdin levels were found when compared to the control group.

2. Group II total protein and albumin levels dropped distinctly when compared with the control group.

3. Ten of group III rats died due to starvation and observations over 3 months were not made. Group III surviving rats had lower properdin levels when compared with controls.

4. Exercised rats showed a significant increase of properdin in both the normal diet and underfed groups.

#### Conclusions

1. The diet, containing 20% of the caloric requirement without restriction of vitamins and minerals administered for 1.5 months, caused significant loss of body weight, followed by significant lowering of total proteins, albumin, and properdin, but no significant changes in globulin fractions.

2. Moderate physical exercise transiently but significantly increased properdin levels in underfed and normally fed rats.

**86. Eberhardt, A., M. Palka, S. Jasser, and S. Lukomski:**  
H. Skowronska, G. Kuszmir-Wojtasik, and S. Lukomski:

Immunological studies of individuals working in high environmental temperature.  
*Acta Physiologica Polonica* 23:291-297, 1972.

#### Authors' abstract

The study investigated blood immunological changes in humans working in high environmental temperatures. The 39 workers were divided into 3 groups. The first group, 15 fitters repairing stoves at temperatures of 40°-120°C, the second group, 14 smelters and the third, 10 common bricklayers were examined to compare them with the main group. The levels of properdin, phagocytic activity

of neutrophilic granulocytes, complement titre, the IgG, IgA, and IgM immunoglobulins content and the titre of specific agglutins were measured. During the 42-day period of work in hot environments, the phagocytic index, IgG, globulins, and titres of specific agglutins were decreased in the stove fitters. The immunity factors became normal during the six weeks of work in the zone of thermal comfort, while only the phagocytic index persisted at a lower level. It was suggested that the stove fitters suffered from diseases more frequently than the other construction workers.

#### 87. Edlund, A.:

The effect of defined physical exercise in the early convalescence of viral hepatitis.

*Scandinavian Journal of Infectious Diseases*  
3:189-196, 1971.

#### Author's abstract

Twenty-three patients with viral hepatitis, mainly of the SH (long incubation) type, underwent quantified physical exercise on an ergometer bicycle during 6 consecutive days in the early convalescence of the disease. None of the patients showed physical signs indicating aggravation of the disease either during the exercise period or at follow-up examinations 1, 2, 4, 8, and 12 weeks after discharge from the hospital. In 19 patients the serum bilirubin and transaminases showed a continuous decrease during the exercise period, while in 4 patients they increased. In all of these 4 patients the values returned to normal during the total period of observation. One patient still showed pathological laboratory test values 12 weeks after the exercise and a further 2 patients stopped coming for follow-up examinations before normal values were regained. All these three patients were narcotic addicts. It appears that physical exercise, started at a relatively early stage (criterion: SGPT  $\leq$  300 IU) in viral hepatitis patients of the category represented by this series, does not result in delayed recovery or deleterious effects on the liver.

#### 88. Edwards, A.J., T.H. Bacon, C.A. Elms,

R. Verardi, M. Felder, and S.C. Knight:

Changes in the populations of lymphoid cells in human peripheral blood following exercise.

*Clinical and Experimental Immunology* 58:420-427, 1984.

#### Authors' abstract

Marked lymphocytosis occurs after exercise. In a study of healthy volunteers this was dominated by one population lacking T cell and B cell determinants and another expressing the Leu 2a phenotype (cytotoxic/suppressor).

Lymphocytes from two individuals were characterized further and a near five-fold increase in cells expressing antigens associated with natural killer (NK) cells (Leu 7 and Leu 11) was noted. In addition, these emergent lymphocytes, unlike most T cells, lacked acid alpha-naphthyl esterase activity. In functional studies, exercise led to significantly greater NK activity but, in spite of altering the distribution of lymphocyte subpopulations, there was no detectable change in the proliferative response to the T cell mitogen, concanavalin A, over a wide range of cell concentration, mitogen dose and time. The numbers of low density macrophages and dendritic cells increased concomitantly with the increase in total lymphocytes. We conclude that exercise increases the proportion of circulating NK cells and cells expressing the Leu 2a phenotype.

## 89. Edwards, H.T. and W.B. Wood:

A study of leukocytes in exercise.  
*Arbeitsphysiologie* 6:73-83, 1932.

### Authors' summary

Hard muscular work is accompanied by a leucocytosis in normal individuals and trained athletes, the leucocytosis in football players often showing an increase of between 200% and 300%. The magnitude of leucocytosis is related to both the duration and the intensity of work. Excitement alone will not cause lymphocytosis which is followed by a polynuclear stage if the work is continued for a long enough time. The average recovery curve exhibits no appreciable drop in leucocyte count during the two hours following a football game unless the player lies down immediately after leaving the field. The absolute lymphocyte count falls rapidly for an hour or more after the player leaves the game. The rapidity of the leucocyte changes, the evidence against leucocytolysis, and the absence of an appreciable increase in the *Schilling-Torgun* "band-form" cells all point toward a storage phenomenon. The bone marrow, spleen, liver, lungs, and organs of internal secretion must be considered as possible reservoirs, although no definite statement can yet be made as to the relative importance of each. The fact that lactic acid, blood sugar, blood pressure, body temperature, and capillary dilation can be ruled out as separate variables directly related to leucocytosis in exercise points toward a stimulus perhaps more complicated than has yet been studied. Any explanation of leucocytosis in exercise involving only a simple physical mechanism cannot at present be considered adequate.

## 90. Egoroff, A.:

Die Veränderung des Blutbildes während der Muskelarbeit bei Gesunden (die Myogene Leukocytose).  
*Zeitschrift für Klinische Medizin* 100:485-497, 1924.  
(*NASA TT F-11, 294, 1967*).

### Author's summary

The blood picture of the present Russian population is different from the norm which prevailed up to 1914, and resembles more what Klieneberger in 1917 classified as "war-time lymphocytosis." This hematological change depends on many factors of general character (nutrition, psychological factors, etc.) and can be regarded as a "social" shift in the blood picture. The myogenic leucocytosis is a true leucocytosis which always takes a regular and uniform course. Its degree and character depends on the quantity and intensity of muscle work and on the physical condition of the individual—that is, his general health, his training, and his fatigue prior to the test. The observed hematological changes increase in proportion to the intensity of the performed work. The myogenic leucocytosis has the following character. There is a fast rise in the leucocytosis which continues to increase for a long time after termination of work. There is initially a relative and an absolute lymphocytosis which, after very strenuous work, changes sharply into a lymphopenia. There is initially a relative and an absolute neutropenia which changes into a marked neutrophilia with a differential shift to the left. There is a relative, and occasionally an absolute, eosinopenia and basopenia. There is a decrease in the number of lymphocytes with azurophile granulation. Occasionally after especially strenuous muscle work, a blood picture is observed which can be regarded as a manifestation of a "myogenic intoxication" of the myeloid tissues.

## 91. Eichner, E.R.:

Exercise, lymphokines, calories, and cancer.  
*The Physician and Sportsmedicine* 15:109-116, 1987.

### Author's abstract

Epidemiological studies suggest that exercise reduces the risk of cancer. The leading studies are reviewed here, along with the underlying animal research and the plausible protective mechanisms in humans. The conclusion, based on the literature, is that exercise may help defend against cancer by preventing obesity, stimulating lymphokines, and/or facilitating other healthful changes in behavior. However, the data are largely preliminary and controversial. Thus, although there is reason to believe that exercise helps prevent

cancer, much more research is needed to prove that it does.

**92. Elliot D.L., L. Goldberg, W.J. Watts, and**

**E. Orwoll:**

Resistance exercise and plasma beta-endorphin/beta-lipotropin immunoreactivity.  
*Life Sciences* 34:515-518, 1984.

**Authors' abstract**

Serum cortisol and plasma beta-endorphin/beta-lipotrophic hormone (LPH) immunoreactivity were measured in five males before and after endurance exercise (treadmill) and burst activity resistance exercise (weight lifting). Mean beta-endorphin/beta-LPH immunoactivity increased significantly following treadmill testing ( $P < 0.05$ ) and weight training ( $P < 0.06$ ). Post-exercise hormonal values were similar for the two activities. The hormonal changes previously reported with endurance activities also occur with burst activity exercise.

**93. Elson, S.H. and W.H. Abelmann:**

Effects of muscular activity upon the acute myocarditis of C3H mice infected with *Trypsionoma cruzi*.  
*American Heart Journal* 69:629-636, 1965.

**Synopsis**

**Purpose** To test the effect of acute infection with *Trypsionoma cruzi* and of forced exertion, singly, and in combination, upon the C3H mouse.

**Methods**

1. Mice were divided into 6 groups:

Group A: Non-infected, no spontaneous running wheel, no forced swimming.

Group B: Infected, no spontaneous running, no forced swimming.

Group C: Non-infected, spontaneous running allowed, no forced swimming.

Group D: Infected, spontaneous running allowed, no forced swimming.

Group E: Non-infected, no spontaneous running, swimming forced.

Group F: Infected, no spontaneous running, swimming forced.

2. Recipient mice were inoculated intraperitoneally with 9,000 organisms.

3. After the day of inoculation, swimming was forced for 60 minutes, 5 times a week, during 6 consecutive weeks.

4. Mice were sacrificed on days 49, 50, and 51, and slide sections of the heart were prepared.

5. The heart was graded 1+, 2+, or 3+ (mild, moderate, or severe) for cellular infiltration.

**Results**

1. Spontaneous activity decreased as parasitemia increased, and increased again as parasitemia subsided.

2. Heart to body-weight ratio increased in swimming alone and by infection alone. The combination of both factors resulted in a significantly higher heart to body-weight ratio than either did alone.

3. Swimming was associated with more severe and diffuse cellular infiltration and with a greater number of parasites in the myocardium.

**Conclusions**

1. Acute myocarditis by *T. cruzi* results in cardiac hypertrophy.

2. *T. cruzi* myocarditis is more severe in mice who were subjected to forced swimming.

**94. Engeset, A., J. Sokolowski, and**

**W.L. Olszewski:**

Variation in output of leukocytes and erythrocytes in human peripheral lymph during rest and activity.  
*Lymphology* 10:198-203, 1977.

**Authors' abstract**

The output of lymphocytes, monocytes, granulocytes, and erythrocytes in peripheral leg lymph from healthy volunteers has been followed during the night and everyday activity, during and after venous stasis, ergometer cycling and warm foot bath and during immobilization in horizontal position over two 24-hour periods. The output of lymphocytes exceeded the output of monocytes and erythrocytes. Granulocytes were not found except immediately after cannulation. The cell output was low during night rest and the horizontal position for 24 hours. After assumption of the upright position the output of lymphocytes increased about 80 times and the output of erythrocytes 40 times, probably because of washout cells accumulated in tissue during rest. During ergometer cycling and venous stasis the output of cells increased and even more in the one-hour rest period following the experiment. During venous stasis the output dropped but increased after the stasis had been released. The pattern of variation in lymphocyte,

erythrocyte, and monocyte output was the same. This indicates that the fluctuation in output depends on variation in blood flow in the tissue. The output of cells during and after heating seems to be dependent also on increased capillary permeability for cells as the output of erythrocytes exceeded the output of lymphocytes. The high erythrocyte/lymphocyte ratio in blood versus a low ratio in lymph shows that these two cell types pass through the capillary wall by different mechanisms.

#### 95. Eriksson, B. and E. Hedfors:

The effect of adrenaline, insulin and hydrocortisone on human peripheral blood lymphocytes studied by cell surface markers.

*Scandinavian Journal of Haematology* 18:121-128, 1977.

##### Authors' abstract

Changes in numbers of peripheral blood lymphocytes from healthy individuals were calculated from samples collected before and after parenteral administration of adrenaline, insulin and hydrocortisone, respectively. A marked increase in circulating lymphocytes was noted in response to adrenaline and insulin. However, subpopulation analysis showed a decrease in the proportion of T-lymphocytes, estimated as cells forming rosettes with sheep red blood cells after incubation in the cold and a corresponding increase in proportion of lymphocytes having receptors for C3 (non-T lymphocytes). In contrast, lymphocyte numbers were unaffected by hydrocortisone. The results indicate that a decreased proportion of circulating T-lymphocytes and an increase of non-T lymphocytes may be the result of adaptive changes in response to various forms of stress and hence is to be expected in several clinical conditions.

#### 96. Eskola, J., O. Ruuskanen, E. Soppi, M.K. Viljanen, M. Järvinen, H. Toivonen, and K. Kouvalainen:

Effect of sport stress on lymphocyte transformation and antibody formation.

*Clinical and Experimental Immunology* 32:339-345, 1978.

##### Authors' abstract

The effect of heavy (marathon, 2.5 hr) and moderate (35 min of running) sport stress on the number and function of lymphocytes, and on the plasma cortisol and leucocyte levels was investigated. Marathon running had a profound effect on the lymphocytes. Though the total number of lymphocytes did not change, their responsiveness to PHA and Con A, and especially to PPD, was

clearly depressed. The suppression of lymphocyte transformation was transient, the recovery occurring in 24 hr. The marathon running had no effect on antibody-forming capacity when the antigen was given immediately after the performance of the marathon, i.e., at the time when the response of lymphocytes to PHA, Con A, and PPD stimulation was impaired. A clear-cut granulocytosis and elevation of plasma cortisol was seen in all the marathon runners. The 35 min of running also resulted in granulocytosis and in an increase of plasma cortisol, but it did not cause any impairment of the lymphocyte function.

#### 97. Espersen, G.T., A. Elbaek, E. Ernst, E. Toft, S. Kaalund, C. Jersild, and N. Grunnet:

Effect of physical exercise on cytokines and lymphocyte subpopulations in human peripheral blood.

*Acta Pathologica, Microbiologica et Immunologica Scandinavica* 98:395-400, 1990.

##### Authors' abstract

To examine the effect of intensive physical exercise on interleukin 2 (IL-2) tumor necrosis factor alpha (TNFa) and lymphocyte subsets, eleven elite and well-conditioned runners were tested in relation to a five-kilometer race. IL-2 was significantly decreased ( $P < 0.01$ ) immediately after the exercise and significantly increased after 24 hours ( $P < 0.05$ ), compared to the pre-exercise values taken at steady state. TNFa was significantly increased after 2 hours ( $P < 0.05$ ), and returned to habitual values after 24 hours. In the steady state at rest, elevation of HLA-DR+ cells was observed in all runners compared with control subjects ( $P < 0.05$ ), indicating a persistent activation of lymphoid cells. In connection with exercise a significant increase in NK cells (CD16+) was observed ( $P < 0.01$ ). The T-helper/T-suppressor (CD4+/CD8+) ratio was significantly reduced in connection with physical activity ( $P < 0.01$ ). In seven runners the ratio was reduced to a value less than one. This decrease was observed immediately after the exercise, followed by increased ratios 2 hours later ( $P < 0.01$ ), due to oppositely directed quantitative changes of the CD4+ and CD8+ cell populations. After 24 hours the ratios returned to habitual levels. Furthermore, we confirmed an increase in the total number of granulocytes in connection with exercise ( $P < 0.01$ ), and observed a decrease in absolute numbers of lymphocytes two hours after exercise ( $P < 0.01$ ). We emphasize the importance of obtaining information about physical activity within the previous 24 hours before measuring white blood cell parameters.

lymphocytes during maximal exercise, except in the case of B lymphocytes (B1+) and NKH1+ cells, and decreases in the absolute and relative number of neutrophils at rest. It remains to be seen how these results can explain the modification of leukocyte activities noted *in vitro* after isolated or chronic exercise.

**105. Ferry, A., B. Weill, I. Amiridis, F. Laziry, and M. Rieu:**

Splenic immunomodulation with swimming-induced stress in rats.  
*Immunology Letters* 29:261-264, 1991.

**Authors' abstract**

In order to determine the effects of swimming-induced stress, young male Wistar rats swam for a single session of 2 h duration, or for one 2-hr session a day for five consecutive days. The absolute number of splenic mononuclear cells and the *in vitro* proliferation of mitogen-stimulated (PHA) T lymphocytes were studied. A single swimming session did not significantly diminish the number of splenic mononuclear cells, but it did significantly reduce splenic T-lymphocyte proliferation. This effect on T-lymphocyte proliferation was significantly blocked, in part, by subcutaneous injection of naltrexone before a swimming session. It was not significantly blocked by pre-exercise oral administration of aminoglutethimide. Repeated swimming sessions induced no significant changes in immune parameters. In conclusion, these data suggest that immunosuppression seen with a single swimming-induced stress period may partly be due to endogenous opioids, and that repetition of the swimming session reduced swimming-induced immunomodulation.

**106. Ferry, A., B. Weill, and M. Rieu:**

Immunomodulations induced in rats by exercise on a treadmill.  
*Journal of Applied Physiology* 69:1912-1915, 1990.

**Authors' abstract**

Various regimens of treadmill exercise (0% slope) were used with rats: 60 min at 15 m/min (T-15), 180 min at 10 m/min (T-10), and 60 min/day at 15 m/min for 6 consecutive days (T-15-6). Exercise resulted in: 1) decreases in the absolute number of mononuclear spleen cells in T-10 rats, 2) significant increases in *in vitro* splenic T-cell blastogenesis in response to phytohemagglutinin in T-10 rats, and 3) significant decreases in T-cell blastogenesis in T-15-6 rats. T-15-6 rats were given aminoglutethimide per os before exercise sessions to study the role of corticosteroids in the alteration of

splenic T-cell blastogenesis. Aminoglutethimide significantly increased the T-cell blastogenesis in these T-15-6 rats compared with those not given aminoglutethimide, whereas it had no effect on immune parameters of sedentary rats. These results showed that immunomodulations in the rat depend on the treadmill exercise regimen employed. If the mechanism of the immunomodulation induced by isolated exercise of long duration are not elucidated, these data suggest that corticosteroids are involved in the alteration in T-cell blastogenesis induced by chronic muscular exercise.

**107. Fiatarone, M.A., J.E. Morely, E.T. Bloom, D. Benton, T. Makinodan, and G.F. Solomon:**

Endogenous opioids and the exercise-induced augmentation of natural killer cell activity.  
*Journal of Laboratory and Clinical Medicine* 112:544-552, 1988.

**Authors' abstract**

Based on prior observations that both  $\beta$ -endorphin and exercise stimulate natural killer (NK) cell activity, we have examined the hypothesis that the release of endogenous opioids during the stress of acute exercise may mediate this NK cell augmentation. Eight healthy young women underwent a maximal bicycle ergometer exercise test with prior *in vivo* administration of a placebo and an opioid antagonist, naloxone (100  $\mu$ g/kg), in a randomized, blind protocol. Exercise after the placebo injection was accompanied by a dramatic rise in NK activity, as well as an increase in the percentage of lymphocytes bearing the NK cell surface markers Leu 11a and Leu 19. Significant stimulation of NK activity was observed with  $\beta$ -endorphin *in vitro* before exercise, but after exercise  $\beta$ -endorphin had a nonsignificant inhibitory effect. When these experiments were carried out in the presence of naloxone *in vivo*, the rise in NK activity after exercise was no longer significant. Naloxone did not significantly alter the rise in Leu 11a+ or Leu 19+ cells after exercise, as compared with the placebo. Finally, when naloxone was given to the subjects beforehand, exercise no longer completely blocked the *in vitro*  $\beta$ -endorphin stimulation of NK cells. In conclusion, our observations that the exercise-induced augmentation of NK activity and the lack of effect of  $\beta$ -endorphin *in vitro* on NK activity after exercise are both significantly attenuated by prior administration of naloxone suggest that the opioid system may play a major role in the modulation of NK cells during physiologic stress.

**108. Fiatarone, M.A., J.E. Morley, E.T. Bloom, D. Benton, G.F. Solomon, and T. Makinodan:**

The effect of exercise on natural killer cell activity in young and old subjects.

*Journal of Gerontology* 44:M37-M45, 1989.

**Authors' abstract**

Alterations in immune function have been commonly reported in elderly persons. We have examined the effect of age on the responsiveness of natural killer (NK) cells to *in vitro* stimulation with recombinant interleukin-2 (rIL-2) and *in vivo* stimulation with exercise in 17 healthy subjects (8 young and 9 old). The old subjects were found to have NK cell numbers and function that were not significantly different from the young subjects at baseline. They also responded as well as the young subjects to rIL-2 stimulation of NK cells *in vitro*. In response to maximal bicycle ergometry exercise, there was a marked rise in NK activity in the old ( $7.52 \pm 1.71$  LU/ $10^6$  pre-exercise vs.  $15.20 \pm 3.27$  LU/ $10^6$  post-exercise,  $P < 0.03$ ) and the young ( $6.29 \pm 0.48$  LU/ $10^6$  vs.  $14.56 \pm 1.86$  LU/ $10^6$ ,  $P < 0.005$ ) subjects. We conclude that healthy elderly subjects increase their NK activity in response to the acute stressor, exercise, at least as effectively as do young subjects.

**109. Field, C.J., R. Gougeon, and**

**E.B. Marliss:**

Circulating mononuclear cell numbers and function during intense exercise and recovery.

*Journal of Applied Physiology* 71:1089-1097, 1991.

**Authors' abstract**

To investigate the effect of intense exercise on immune function, 12 healthy males ( $26 \pm 1$ yr) underwent cycle exercise to exhaustion at 80% maximum work load. One hour later, six of the subjects underwent a second identical bout. Blood was drawn preexercise (C), at exhaustion (Ex-1, Ex-2), and at 1 h of recovery (Rec-1, Rec-2). At Ex-1 and Ex-2 total leukocytes (monocytes, neutrophils, and lymphocytes) increased significantly ( $P < 0.05$ ), and all returned to C levels by Rec-1 except lymphocytes, which were lower than at C. At Rec-2 total leukocytes remained higher ( $P < 0.05$ ) than at C, primarily because of elevated neutrophil counts. Phenotype analysis indicated a 2.5-fold increase in CD16+ (natural killer) cells at Ex-1 and a decreased primarily in CD4+ (T-helper) cells. All phenotype changes returned to C levels at Rec-1. At Ex-1 the *in vitro* mitogenic responses to concanavalin A, phorbol myristate acetate-ionomycin, phytohemagglutinin, and pokeweed mitogen

decreased ( $P < 0.05$ ) but returned to levels not different from C at Rec-1. Both the *in vitro* percent specific lysis of a target natural killer cell (K562) and the lytic activity per cell increased ( $P < 0.05$ ) in peripheral mononuclear cells at Ex-1, returning to C levels at Rec-1. The total leukocyte counts with exercise were significantly correlated with plasma epinephrine concentration, and a causal effect is thus possible. Such acute changes in numbers and function of circulating cells of the immune system may possible have functional and clinical correlates.

**110. Fitzgerald, L.:**

Overtraining increases the susceptibility to infection. *International Journal of Sports Medicine* 12:S5-S8, 1991.

**Author's abstract**

Recent research studies and other evidence suggest that although moderate exercise is good for the immune system, the demanding training programs of many top athletes may suppress the immune system and thereby increase susceptibility to infections. A number of top athletes have suffered from unusual infections normally associated with immune deficiency, and immune abnormalities have been demonstrated in resting samples from top athletes. Studies from several exercise laboratories have shown that after a single exhausting exercise session there is temporary immune depression, with marked changes in numbers and functional capacities of lymphocytes. These changes, which last for up to several hours, are seen in athletes and untrained individuals. In several studies in the United States, students who were very active in sports have been shown to be more susceptible to infections than their less active colleagues. Exercising hard during the incubation phase of an infection can increase the severity of the illness. This article examines the evidence, discusses possible mechanisms, and considers the implications.

**111. Foster, N.K., J.B. Martyn, R.E. Rangno,**

**J.C. Hogg, and R.L. Pardy:**

Leukocytosis of exercise: role of cardiac output and catecholamines.

*Journal of Applied Physiology* 61:2218-2223, 1986.

**Authors' abstract**

The effect of propranolol (5 mg iv) on the leukocytosis of exercise was studied in seven normal young males. Leukocyte counts, plasma norepinephrine (NE), epinephrine (E), and cardiac output were measured at rest and in the steady state of several submaximal work loads



compared to recordings on occasion III. In the female patients the systolic blood pressure (BP, lowest and mean) during standing was similar on occasions I and III, while the male patients showed a significant decrease after illness. The standing diastolic BP was significantly lower after illness/bed rest in the male patients and control subjects but not in the female patients who maintained the same level. The orthostatic dysfunction, expressed in terms of HR response, was significantly more pronounced in those patients who suffered from pneumonia than in the other patients. Respiratory rate and ventilation volume tended to be higher on occasion I than on succeeding occasions, but bed rest alone had no effect on these variables. For the same absolute amount of work, oxygen uptake was lower on occasion I than on occasion III, most differences being probably significant. The blood lactate concentration, determined after the same absolute amount of work, was significantly higher on occasion I than on succeeding occasions in both patients and control subjects. An inverse pattern was seen when the working capacity was expressed as percentages of the values of occasion III and related to a given lactate level ( $W_{lact}$ ). On occasion I and II both the  $W_{lact}$  fraction of the female patients were significantly lower than those of the control subjects, indicating a greater relative deterioration in the female patients. Similarly, these values were lower in the male patients than in the control subjects, but not significantly so. There were no significant differences in the  $W_{lact}$  fraction when compared to the  $W_{150}$  fraction on occasions I or II, in each series of subjects, indicating that the deterioration was roughly parallel when expressed in "circulatory" or in "metabolic" terms. In conclusions, the results confirm that cardiovascular dysfunction occurs in patients confined to bed with acute febrile infections. Part of the deterioration is caused by the clinical bed rest but it is relevant to conclude that acute febrile infection as such brings about an additional impairment. Thus, in the present study, with bed rest effects eliminated, orthostatic dysfunction has been shown to occur. On the other hand, the physical working capacity, expressed in different terms, was not significantly reduced by illness as such (except in pneumonia patients) although a consistent trend suggesting an additional effect added to that caused by bed rest alone was demonstrated. Heart volume was not significantly altered.

## 116. Friman, G.:

Effect of acute infectious disease on human isometric muscle endurance.

*Uppsala Journal of Medical Sciences* 83:105-108, 1978.

### Author's abstract

Capacity for isometric endurance work of different muscle groups was recorded in 32 male patients suffering a variety of acute infectious diseases, predominantly of viral or mycoplasmal aetiology. Recordings were performed after abatement of fever, and 1 and 4 months thereafter. Control measurements took place 1 year later. As a result of the illness the subjects' endurance capacity was reduced to 82.5-86.9% of the control values. Complete recovery was attained later than 4 months after the acute disease. In 21 healthy male control subjects confined to bed for the same period of time as the patients, no reduction of endurance capacity was observed as a result of bed rest. The illness-induced and long-lasting impairment of static endurance after acute febrile infections might be related to observations in similar patients of reduced activity in muscle tissue of glyceraldehyde-3-phosphate dehydrogenase being a key enzyme in glycolysis.

## 117. Friman, G.:

Effect of acute infectious disease on isometric muscle strength.

*Scandinavian Journal of Clinical and Laboratory Investigation* 37:303-308, 1977.

### Author's abstract

Isometric strength of different muscle groups was recorded in thirty-nine patients suffering various acute infectious diseases, predominantly of viral or mycoplasma aetiology. Recordings were performed after subsidence of fever, and 1 and 4 months thereafter. A control group of twenty-two healthy men, confined to bed for the same period of time as the patients, were investigated at the same time intervals. In addition, control measurements were performed after 1 year in the patients, and prior to bed rest in the control subjects. As a result of illness muscle strength was decreased significantly to 85.4-95.3% of that recorded at 4 months. In the control subjects strength did not change significantly, the corresponding percentages being 96.3-102.5. Thus, the present data indicate that these illnesses in themselves may bring about isometric strength reduction.

**118. Friman, G., N.-G. Ilbäck, W.R. Beisel, and D.J. Crawford:**

The effects of strenuous exercise on infection with *Francisella tularensis* in rats.  
*Journal of Infectious Diseases* 145:706-714, 1982.

**Authors' abstract**

To investigate the effects of strenuous forced exercise on the course and complications of a bacterial infection and on myocardial responses and performance capacity, rats with tularemia (characterized by pyogranulomatous hepatic and splenic lesions) were exercised by swimming on days 0-6 of infection. Levels of glutamic oxaloacetic and pyruvic transaminases in plasma, densities of pyogranulomatous lesions, and bacterial counts in blood, liver, and spleen were similar in exercising and resting rats. Although a few exercising rats showed an unusual dissemination of infection, the antibody responses were similar in rest and exercise. Plasma concentrations of  $\beta$ -glucuronidase, lysozyme, and 2-macrophetoprotein were higher with exercise, a result that indicated that more vigorous stress responses were elicited with exercise than with infection alone. Physical performance capacity was reduced by the infection, but forced daily exercise limited this reduction substantially and counteracted the myocardial protein-degrading effects of infection. Thus, exercise evoked normal training responses even during this generalized infection.

**119. Friman, G., N.-G. Ilbäck,**

**D.J. Crawford, and H.A. Neufeld:**

Metabolic responses to swimming exercise in *Streptococcus pneumoniae* infected rats.  
*Medicine and Science in Sports and Exercise* 23:415-421, 1991.

**Authors' abstract**

The present study was performed to determine whether alterations in fuel reserves or energy substrate utilization might explain the performance decrements that occur in bacterial infections. Male Fisher-Dunning rats were studied at 24, 48, and 72 hours after inoculation with *Streptococcus pneumoniae*. Rats were either sedentary or subjected to a 2 hour swimming session at these three time points (N = 10 in each group). A more than 60% reduction ( $P < 0.01$ ) in performance capacity was observed on day 3 of infection compared with that in non-infected controls. This infection in the rat is characterized by fever ( $P < 0.01$ ), depression of plasma zinc ( $P < 0.01$ ) and free fatty acid (FFA) levels ( $P < 0.01$ ), inhibition of the two- to threefold increase in fasting ketonemia, and a decreased (NS) insulin:glucagon ratio, indicating a

catabolic state. Glycogen stores were reduced in the heart (47%), liver (43%), and skeletal muscles (39%) but not in the carcass. Superimposed exercise resulted in a further reduction but not depletion of liver, muscle, and carcass glycogen stores, a less pronounced lactic acid accumulation, and a lower oxygen debt. However, plasma FFA and ketone body levels were still maintained or even elevated, suggesting that fat is supplied as fuel during swimming exercise in this infection. Thus, results indicate that unavailability of energy substrates or lactacidosis is not limiting for performance capacity during this severe infection.

**120. Friman, G., H.H. Schiller, and M.S. Schwartz:**

Disturbed neuromuscular transmission in viral infections.

*Scandinavian Journal of Infectious Diseases* 9:99-103, 1977.

**Authors' abstract**

Fourteen subjects with influenza or echovirus infection, all suffering myalgia, and 9 subjects with mumps, in whom this symptom was lacking, were investigated with single fiber electromyography (EMG) in the acute phase and during convalescence to reveal a possible disturbance in neuromuscular transmission. In both groups about the same percentage of the potential pairs studied showed abnormal transmission characteristics in the acute phase. Two weeks after the acute infection, this percentage had decreased significantly in the group with myalgia, whilst in the non-myalgia group it was still at the same level. However, on both occasions of investigation and in both groups the percentages were substantially greater than those recorded in healthy individuals. This study demonstrates that acute febrile infections may adversely affect neuromuscular transmission in previously healthy human subjects. The effects observed might offer an explanation for the accentuated muscular weakness in association with infections in patients with an already low safety margin of neuromuscular transmission, e.g., in myasthenia gravis.

**121. Friman, G., J.E. Wright, N.G. Ilbäck, W.R. Beisel, J.D. White, D.S. Sharp, E.L. Stephen, W.L. Daniels, and J.A. Vogel:**

Does fever or myalgia indicate reduced physical performance capacity in viral infections?  
*Acta Medica Scandinavica* 217:353-361, 1985.

**Authors' abstract**

To study prospectively the effects of a brief febrile viral infection on parameters of muscle and circulatory

function, seven volunteers were inoculated with sandfly fever virus and two control subjects with sterile saline. During, but not after fever, decreased isometric and dynamic strength and endurance were recorded in various muscles. Impairment could not be explained by altered activities of relevant muscle enzymes in serum or muscle tissue or by altered muscle ultrastructure, but correlated with the severity of perceived symptoms, including myalgia, as rated by each subject. Compared to baseline, cardiac stroke volume was lower during and after fever. During fever, an increased heart rate maintained cardiac output at pre-inoculation values, whereas cardiac output fell in early convalescence. This decrease in cardiac output correlated significantly with the severity of fever. Thus, in brief viral infections a transient impairment of muscle performance capacity is correlated to subjective symptoms such as myalgia, rather than to fever, whereas a decreased cardiac output following such infections seems to be associated with the fever reaction.

**122. Frisch, R.E., G. Wyshak, N.L. Albright, T.E., Albright, and I. Schiff:**

Lower prevalence of non-reproductive system cancers among female former college athletes.  
*Medicine and Science in Sports and Exercise* 21:250-253, 1989.

**Authors' abstract**

The prevalence (lifetime occurrence) rates of cancers of nonreproductive organs and tissues were determined for 5,398 living alumnae, 2,622 of whom were former college athletes and 2,776 who had been nonathletes, from data on medical history, reproductive history, athletic training, and diet. The non-reproductive system cancers were divided into two classes: class I, which included cancers of the digestive system, thyroid, bladder, lung, and other sites and hematopoietic cancers (lymphoma, leukemia, myeloma, and Hodgkin's disease), and class II, which included skin cancers and cutaneous melanoma. The former college athletes had a significantly lower prevalence of class I cancers compared to the nonathletes; the age-adjusted relative risk (RR) equals 3.34, 95% confidence limits (1.35, 8.33),  $P = 0.009$ . In contrast, the prevalence rates of malignant melanomas and skin cancers did not differ significantly between the former athletes and nonathletes. The age-adjusted RR did not differ from 1.0. The lower prevalence rate of class I cancers among the former athletes is in accord with previous findings of a significantly lower prevalence rate of breast cancer and cancers of the reproductive system among former college athletes compared to nonathletes.

**123. Frisch, R.E., G. Wyshak, N.L. Albright, T.E. Albright, I. Schiff, K.P. Jones, J. Witschi, E. Shiang, E. Koff, and M. Margulio:**

Lower prevalence of breast cancer and cancers of the reproductive system among former college athletes compared to non-athletes.  
*British Journal of Cancer* 52:885-891, 1985.

**Authors' abstract**

The prevalence (lifetime occurrence) rate of cancers of the reproductive system (uterus, ovary, cervix and vagina) and breast cancer was determined for 5,398 living alumnae, 2,622 of whom were former college athletes and 2,776 non-athletes, from data on medical and reproductive history, athletic training and diet. The former athletes had a significantly lower risk of cancer of the breast and reproductive system than did the non-athletes. The relative risk (RR), non-athletes/athletes, for cancers of the reproductive system was 2.53, 95% confidence limits (CL) (1.17, 5.47) The RR for breast cancer was 1.86, 95 % CL (1.00, 3.47). The analysis controlled for potential confounding factors including age, family history of cancer, age of menarche, number of pregnancies, use of oral contraceptives, use of oestrogen in the menopausal period, smoking, and leanness. Of the college athletes, 82.4% had been on pre-college teams compared to 24.9% of the college non-athletes. We conclude that long term athletic training may lower the risk of breast cancer and cancers of the reproductive system.

**124. Frohlich, J., G. Simon, A. Schmidt, T. Hitschhold, and M. Bierther:**

Disposition to infections of athletes during treatment with immunoglobulins.  
*International Journal of Sports Medicine* 8:119, 1987.

**Authors' abstract**

In a double blind study the effect of intramuscular applications of human immunoglobulins on disposition to infections of athletes was investigated. Twenty swimmers (mean age  $19.1 \pm 0.6$  years) belonging to the Sports School of the German Armed Forces were examined during the period (of time) from January to June. In February the verum group ( $V, n = 10$ ) received an initial dose of 1.6 g immunoglobulin i.m., thereafter 3 times 0.8 g with 4 week intervals. At the same dates, the placebo group ( $P, n = 10$ ) received same quantities of physiological saline solution. Every 4 weeks before start of treatment, before each immunoglobulin- or

placebo-application—and at the manifestation of an acute infection blood was drawn for determination of blood cell sedimentation, erythrocytes, leukocytes, acetate phase proteins, complement c3c and c4, alpha 2-macroglobulin, total serum protein, and immunoglobulin-levels. The most important results were: (1) The same number of infections occurred in both groups during the period of treatment (V: 15, P: 14). (2) In contrast, the duration of the infections—determined by disease days—was three times shorter in the verum group than in the placebo group (V: 78, P: 232). Differences and changes of the serum parameters influenced by the treatment with immunoglobulins and by infections are discussed.

## 125. Gabriel, H., A. Urhausen, and W. Kindermann:

Circulating leukocyte and lymphocyte subpopulations before and after intensive endurance exercise to exhaustion.

*European Journal of Applied Physiology* 63:449-457, 1991.

### Authors' abstract

Seventeen healthy cyclists [age 20.8 (SD 4.8) years; body mass 68.3 (SD 7.7) kg; body fat 11.4 (SD 7.4) ml kg<sup>-1</sup> min<sup>-1</sup>] conducted intensive endurance exercise to exhaustion (stress test, ST) on a cycle ergometer at 110% of their individual anaerobic threshold [Than, individual; exercise intensity, 3.97 (SD 0.6) W/kg; duration, 23.9 (SD 8.3) min; maximal lactate concentration, 7.39 (SD 2.59) mmol l<sup>-1</sup>]. The distribution of leukocyte subpopulations was measured by flow cytometrically: before, immediately after (0), 5 (+5), 30 (+30) and 60 (+60) min after ST. The lymphocytes (0 min) and granulocytes (+60 min) were mainly responsible for the increase of leucocytes. Lymphocytes were significantly lower at +30 and +60 min than before. CD3<sup>+</sup>CD16/CD56<sup>+</sup> (+480%) and CD8<sup>+</sup> lymphocytes (+211%) increased at 0 min more than the other lymphocyte subpopulations (CD3<sup>+</sup> cells, +100%; CD4<sup>+</sup> cells +56%; CD19<sup>+</sup> cells, +64%). CD3<sup>+</sup>CD16/CD56<sup>+</sup> and CD8<sup>+</sup> cells also were mainly responsible for the decreased values of lymphocytes at +30 min and +60 min compared to before. At 0 min naive CD8<sup>+</sup> cells (CD45RA<sup>+</sup>, CD45RO<sup>-</sup>) increased more than memory CD8<sup>+</sup> cells (CD45RA<sup>-</sup>, CD45RO<sup>+</sup>). Changes of naive and memory CD4<sup>+</sup> cells did not differ. All lymphocyte subpopulations, in particular CD8<sup>+</sup> and CD3<sup>+</sup>CD16/CD56<sup>+</sup> cells, decreased rapidly between 0 and 5 minutes. We conclude that an intensive endurance exercise to exhaustion causes a mobilization of lymphocytes, especially of natural killer cells (CD3<sup>+</sup>CD16/CD56<sup>+</sup>) and naive, unprimed CD8<sup>+</sup> cells

(CD45RA<sup>+</sup>, CD45RO<sup>-</sup>) which may be transported to injured muscles. The decreased cell numbers of the latter subpopulations are possibly one reason for the susceptibility to infections during the first hours after exercise. Furthermore, an exact definition of the intensity of exercise and times of taking blood is essential for comparing results describing cell parameters during or after exercise.

## 126. Gallal, O., M.C. Michel, and O.-E. Brodde:

Dynamic exercise induced  $\beta$ -adrenoreceptor changes in human lymphocytes: a  $\beta$ 2-adrenoreceptor mediated process.

*Naunyn-Schmiedeberg's Archives of Pharmacology* 330:R60, 1985.

### Authors' abstract

Acute stimulation of the sympathetic activity by dynamic exercise on a bicycle (80% of maximum heart rate) for 15 min caused in healthy male volunteers an about 100% increase in lymphocyte  $\beta$ 2-adrenoreceptor density (assessed by (-)-125-iodocyanopindolol binding) and -responsiveness (lymphocyte cAMP responses to 10 $\mu$ M isoprenaline). To gain further insights into the mechanism underlying this effect, the influence of propranolol and the selective  $\beta$ 1-antagonist bisoprolol (bis(1-(4-((2-isopropoxyethoxy)-methyl)-phenoxy)-3-isopropylamino-2-propanol) on exercise induced lymphocyte  $\beta$ 2-adrenoreceptor changes was studied. Pretreatment of the volunteers with propranolol (5 mg i.v. 45 min prior to exercise) completely abolished exercise induced increases in S2-adrenoreceptor density and -responsiveness, whereas pretreatment with bisoprolol (2.5 mg i.v. 30 min prior to exercise) had no effect. In the same dose, however, bisoprolol suppressed isoprenaline evoked increase in plasma renin activity mediated by intrarenal  $\beta$ 1-adrenoreceptor mediated effects. It is concluded, therefore, that dynamic exercise induced increased in lymphocyte  $\beta$ 2-adrenoreceptor density and responsiveness is a  $\beta$ 2-adrenoreceptor dependent process.

127. Galun, E., R. Burstein, E. Assia, I. Tur-Kaspa, J. Rosenblum, and Y. Epstein:

Changes of white blood cell count during prolonged exercise.

*International Journal of Sports Medicine* 8:253-255, 1987.

**Authors' abstract**

Leukocytosis was postulated to accompany short- and medium-length exercise; in this report, we have studied the changes in leukocyte count during and following prolonged exercise. White blood cell (WBC) counts were obtained in 15 endurance-trained subjects before, during, and at a recovery period after an ultralong exercise (120 km march), lasting 24 hours. WBC counts increased after a 16-hour march from a baseline value of  $8.5 \pm 0.3 \cdot 10^9 \text{ l}^{-1}$  to  $11.3 \pm 0.8 \cdot 10^9 \text{ l}^{-1}$  ( $P < 0.05$ ) and then declined to  $7.1 \pm 0.9 \cdot 10^9 \text{ l}^{-1}$  after a 24-hour march with no further significant changes during a 64 hours of recovery. These observations were supported by previous findings in three separate marches performed by a second group (40, 70, and 120 km). A parallel increase in plasma creatine phosphokinase activity from  $127 \pm 4.4/\mu\text{l}$  to  $539 \pm 106.3/\mu\text{l}$  was observed after a 16-hour march ( $P < 0.01$ ), indicating muscle cell damage. Our findings suggest that in extremely long marches, WBC counts return to baseline values before exercise is terminated. This phenomenon may reflect WBC infiltration to damaged muscle tissue.

128. Gambert, S.R., T.L. Garthwaite, C.H. Pontzer, E.E. Cook, F.E. Tristani, E.H. Duthie, D.R. Martinson, T.C. Hagen, and D.J. McCarty:

Running elevates plasma  $\beta$ -endorphin immunoreactivity and ACTH in untrained human subjects.

*Proceedings of the Society for Experimental Biology and Medicine* 168:1-4, 1981.

**Authors' abstract**

Twenty minutes of submaximal treadmill running was associated with an elevation in plasma levels of  $\beta$ -endorphin immunoreactivity ( $P < 0.02$ ). This increase was greater in men ( $14.9 \pm 3.4 \text{ fmole/ml}$ ) than women ( $2.6 \pm 1.2 \text{ fmole/ml}$ ) ( $P < 0.05$ ). Plasma levels of ACTH and growth hormone also increased after running. ACTH increased more in men ( $7.8 \pm 1.1 \text{ fmole/ml}$ ) than in women ( $1.1 \pm 0.44 \text{ fmole/ml}$ ) ( $P < 0.02$ ). There was a similar growth hormone response in both sexes. No correlation can at this time be made with levels in the

central nervous system. Changes in plasma levels of  $\beta$ -endorphin immunoreactivity may be responsible for some of the euphoria and analgesia anecdotally associated with running.

129. Gardner, H.T., R.A. Rovelstad, D.J. Moore, F.A. Streifeld, and M. Knowlton:

Hepatitis among American occupation troops in Germany: A follow-up study with particular reference to interim alcohol and physical activity. *Annals of Internal Medicine* 30:1009-1019, 1949.

**Authors' abstract**

One hundred and fourteen American soldiers were studied six months to one year after hospitalization for an attack of infectious hepatitis acquired in Germany. Of these, 46 had been discharged from the hospital with slight residual abnormalities, and 68 as presumably cured. Only slight differences were noted between the two groups on reexamination after the interval, and there were relatively more residuals present in the group discharged as presumably cured than in those discharged with slight residuals. When reexamined with particular reference to their interim activity and alcohol, it appeared that neither of these factors played a significant role in the appearance of residuals in either group.

130. Gatmaitan, B.G., J.L. Chason, and A.M. Lerner:

Augmentation of the virulence of murine coxsackie virus B-3 myocardiopathy by exercise.

*Journal of Experimental Medicine* 131:1121-1136, 1970.

**Synopsis**

**Purpose** To investigate the effect of swimming exercise upon murine coxsackievirus B-3 myocardiopathy.

**Methods**

1. At 14 days of age, 6 groups of 36 mice were formed.

Group I mice; infected and made to swim.

Group II mice; infected and not made to swim.

Group III mice; not infected and made to swim.

Group IV mice; not infected and not made to swim.

Group V mice; infected but not forced to swim until 9 days later.

Group VI mice; not infected but not forced to swim until 9 days later.

2. Mice were inoculated intracerebrally and intraperitoneally.
3. Six mice from each group were sacrificed by exsanguination on days 3, 6, 9, 13, 20, and 40 mice after inoculation.
4. The degree of tissue involvement was graded for single block organ analysis.
5. Virology titers were done in positive cultures.

#### Results.

1. In infected mice, swimming increased mortality from 5.5% to 50%; their hearts were dilated and necrotic, and ratios of mean heart to body weight increased.
2. Virtually every myocardial fiber showed pathological change as opposed to 1/4 to 1/2 of myocardial involvement when infection was not accompanied by swimming.
3. When swimming was initiated while viral replication in heart was decreasing, mortality increased 13.8% over non-exercised controls.
4. Inflammatory lesions in pericardial fat were increased by swimming.

#### Conclusions

Coxsackie virus B-3 multiplication in the heart was augmented when infection was accompanied by swimming. However, when swimming was initiated while virus replication in the heart was waning, the duration of multiplication of virus was not increased by swimming.

### 131. Gille, G., O. Ringertz, and

#### B. Zetterberg:

Serum hepatitis among Swedish track-finders.

II. A clinical study.

*Acta Medica Scandinavica* 182:129-135, 1967.

#### Authors' abstract

During 1957-1962 an outbreak of hepatitis involving 568 cases occurred among Swedish track-finders. Epidemiological data suggested that the disease was serum hepatitis. The clinical features of the disease were studied in 320 cases. The onset of the disease was found to have been insidious in most cases. A temperature of 38°C or more was found in only 3% of the cases. The clinical symptoms, laboratory results and morbid anatomy corresponded in all respects with those of viral hepatitis. Only one case was fatal.

### 132. Gimenez, M., T. Mohan-Kumar, J.C. Humbert, N. De Talance, and

#### J. Buisine:

Leukocyte, lymphocyte and platelet response to dynamic exercise.

*European Journal of Applied Physiology* 55:465-470, 1986.

#### Authors' abstract

The influence of work intensity and duration on the white blood cell (WBC), lymphocyte (L) and platelet (P) count responses to exercise was studied in 16 trained subjects ( $22 \pm 5.4$  years,  $\bar{X} \pm SD$ ). They performed three cycloergospirometric protocols: A) 10 min at 150 W followed by a progressive test (30 W/3 min) till exhaustion; B) constant maximal work ( $\dot{V}O_2$ max); C) a 45 minute Square-Wave Endurance Exercise Test (SWEET), (n = 5). Arterial blood samples were taken: at rest, submaximal and maximal exercise in A; maximal exercise in B; 15<sup>th</sup>, 30<sup>th</sup>, and 45<sup>th</sup> min in the SWEET. Lactate,  $[H^+]$ ,  $PaCO_2$ ,  $PaO_2$ ,  $[Hct]$ , Hb, cortisol, ACTH, total platelet volume (TPV), total red blood cell (RBC), WBC, L, and P were measured. At 150 W, WBC, L, P, and TPV increased.  $\dot{V}O_2$ max did not differ between A and B, but a difference was found in total exercise time (A =  $25 \pm 3$  min; B =  $7 \pm 2$  min,  $P < 0.001$ ). In A, at  $\dot{V}O_2$ max, the increase was very small for Hct,  $[Hb]$ , and RBC (10%), in contrast with large changes for WBC (+93%), L (+137%), P (+32%), TPV (+35%),  $[H^+]$  (+39%), lactate (+715%), and ACTH (+95%). At  $\dot{V}O_2$ max there were no differences in these variables between A and B. During the SWEET: WBC, L, P, TPV and ACTH increased at the 15<sup>th</sup> minute as much as in  $\dot{V}O_2$ max, but no difference was observed between the 15<sup>th</sup>, 30<sup>th</sup> and 45<sup>th</sup> min, except for ACTH which continued to rise; the lactate increase during the SWEET was about half (+341%) the value observed at  $\dot{V}O_2$ max, and  $[H^+]$  did not vary with respect to values at rest. The data show that the increase in WBC, L, P, and TPV is small in submaximal exercise but larger at  $\dot{V}O_2$ max and during the SWEET; high intensity plays a greater role than the total time of exercise in the variation, and haemoconcentration, cortisol and acidosis seem to have little influence.

**133. Gimenez, M., T. Mohan-Kumar, J.C. Humbert, N. De Talance, M. Teboul, and F.J.A. Belenguer:**

Training and leucocyte, lymphocyte, and platelet response to dynamic exercise.

*Journal of Sports Medicine* 27:172-177, 1987.

**Authors' abstract**

To analyze the influence of training in leucocyte, lymphocyte and platelet count responses to exercise, twenty nine normal male subjects: 13 untrained (U) and 16 trained (T), performed an exercise, on a cycle ergometer, in which a submaximal load of 40 W (U) or 150 W (T) was maintained for ten minutes and then the load was increased by 30 W every minute until the maximal work ( $\dot{V}O_2$  max) was obtained. Arterial blood samples were taken at rest, submaximal and maximal exercise. Lactate,  $[H^+]$ ,  $PaCO_2$ ,  $PaO_2$ , Hct, [Hb], platelets (P), total platelet volume (TPV), total white (WBC) and red (RBC) blood cell count, lymphocytes (L), cortisol and ACTH were measured. Maximal work load ( $\bar{X} \pm SD$ ) ( $U = 238 \pm 28$ ;  $T = 308 \pm 30$  W,  $P < 0.001$ ), and total exercise time ( $U = 30 \pm 3.2$ ;  $T = 25 \pm 2.8$  min,  $P < 0.001$ ) were different between both groups. From rest, an increase was observed, at submaximal exercise, in WBC ( $U = +20\%$ ;  $T = +32\%$ ), lymphocytes ( $U = +21\%$ ;  $T = +37\%$ ), platelets ( $U = +8\%$ ;  $T = +10\%$ ) and TPV ( $U = +7\%$ ;  $T = +11\%$ ). At  $\dot{V}O_2$  max the increase was very low for Hct ( $+10\%$ ), [Hb] ( $+7.5\%$ ) and RBC ( $+8\%$ ) in contrast with large changes for WBC ( $U = +76\%$ ;  $T = +93\%$ ), L ( $U = +105\%$ ;  $T = +137\%$ ), ( $U = +29\%$ ;  $T = +32\%$ ,  $P < 0.01$ ), and ACTH ( $U = +136\%$ ;  $T = +95\%$ ). Moreover TPV was larger at rest in T than in U subjects ( $P < 0.01$ ). The data observed suggests that: the increase in WBC and L is not different between T and U subjects either at submaximal or maximal exercise; on the contrary TPV and platelet count were higher in T subjects at rest and at  $\dot{V}O_2$  max; cortisol and lactic acidosis seem to have light influence in these variations, which are related more to the higher level of exercise performed by T subjects.

**134. Glezen, W.P., J.L. DeWalt,**

**R.L. Lindsay, and H.C. Dillon, Jr.:**

Epidemic pyoderma caused by nephritogenic streptococci in college athletes.

*Lancet* 1:301-304, 1972.

**Authors' abstract**

An epidemic of streptococcal pyoderma occurred among football players at the University of North Carolina. Lesions consisted of infected abrasions and minor

lacerations, many of which were superficial and did not produce enough discomfort to cause individuals to seek medical care. The epidemic strain was an M-type 2 streptococcus with antigenic characteristics similar to those recently associated with significant numbers of cases of acute glomerulonephritis following

pyoderma in children. The antistreptolysin-O and anti-deoxyribonuclease-B responses to infection were slight. Nephritis was not detected among the North Carolina football players, as evidenced by normal urinalysis, the absence of clinical disease, and normal serum-complement (C3) levels. The absence of nephritis possibly can be explained by the minor nature of infections, the relatively mild immune response, prompt specific therapy, and, perhaps, the age of those affected.

**135. Gmünder, F.K., G. Lorenzi, B. Bechler, P. Joller, J. Müller, W.H. Ziegler, and A. Cogoli:**

Effect of long-term physical exercise on lymphocyte reactivity: Similarity to spaceflight reactions.

*Aviation, Space and Environmental Medicine* 59:146-151, 1988.

**Authors' abstract**

The response of critical immunological parameters in seven athletes to the sustained physical stress of marathon running was assessed. Variables analysed were the responsiveness of lymphocytes (measured as mitogenic response to concanavalin A), the numbers of lymphocytes, their subsets, and leukocyte numbers. In addition blood levels of cortisol, epinephrine, and norepinephrine were determined. After the run, lymphocyte responsiveness was severely depressed to 1-70% of the resting values, even though the lymphocyte counts did not change. Leukocyte counts were elevated 2.8-fold. No dramatic changes were found within the lymphocyte subsets, although an increase in pan-T-cells and the helper/inducer subset 2 d after the run was significant. In addition, the numbers of B-cells decreased significantly. No change was observed within the suppressor/cytotoxic subset. Cortisol increased 2.1-fold, epinephrine 3.2-fold, and norepinephrine 2.7-fold. All these parameters returned to baseline values within 2 days. These data were compared with data obtained during and after spaceflight. We conclude that prolonged physical stress of marathon running induces changes in immunological responsiveness that are strikingly similar to those arising from the stress of spaceflight.

**136. Good, R.A. and G. Fernandes:**

Enhancement of immunologic function and resistance to tumor growth in Balb/C mice by exercise.

*Federation Proceedings* 40:1040, 1981.

**Authors' abstract**

Regular moderate exercise is known to aid in resistance to infection and development of diseases of aging. In order to understand the effect of daily exercise on immunological analyses, 8-week old Balb/c female mice were placed in the following experimental groups: 1) regular exercise—forced to run on a controlled rodent treadmill for 30-45 min/day at a speed of 0.8-1.2 miles per hour for five days a week (constant running maintained by avoidance of mild electric shock); 2) a group exposed to equal amounts of shock alone; and 3) non-exercised, non-shocked controls. At 4, 6, and 8 weeks after the start of the experiment, mice from the three groups were immunized with 0.2 cc of 20% sheep red blood cells (SRBC). Four days after immunization spleen cells were collected to measure plaque forming cell (PFC) responses to SRBC and *in vitro* responses to the mitogens PHA, Con A, and LPS. No differences among the groups were seen in the mitogenic responses. The exercised mice demonstrated increased PFC responses and exhibited a gradual decrease in thymic size. Lastly, when animals were immunized with  $1 \times 10^5$  syngeneic RLo1 tumor cells after 8 weeks of the various regimens, a significant delay in tumor growth was observed in the exercise group. Thus, it appears that exercise significantly alters immunologic response in mice.

**137. Goodwin, J.S., S. Bromberg, C. Staszak,**

**P.A. Kaszubowski, R.P. Messner, and**

**J.F. Neal:**

Effect of physical stress on sensitivity of lymphocytes to inhibition by prostaglandin E<sub>2</sub>.  
*Journal of Immunology* 127:518-522, 1981.

**Authors' abstract**

Physical stress is associated with depressed cellular immune function. We have found that lymphocytes from subjects undergoing either of 2 stressful events, cardiac surgery or childbirth, are more sensitive to inhibition by PGE<sub>2</sub>. For example, the concentration of PGE<sub>2</sub> required for 50% inhibition of <sup>3</sup>H-thymidine incorporation (ID<sub>50</sub>) into phytohemagglutinin-stimulated lymphocytes from patients undergoing cardiac surgery went from  $1.5 \times 10^{-8}$  M on the day before surgery to  $3 \times 10^{-9}$  M on the day after surgery. This increase in sensitivity to PGE<sub>2</sub> was accompanied by a significantly decreased

lymphocyte proliferative response (27 to 68% of control, depending on mitogen dose) and a 50% increase in the percentages of E rosette-positive cells with receptors for the Fc portion of IgG. The increased sensitivity to PGE and the depressed mitogen responses returned to pre-operative values by day 10. The depressed mitogen responses of the post-operative patients were completely restored to normal by removal of glass-adherent cells before culture. In addition, the responses of the post-operative patients and the women in labor were partially restored by the addition of indomethacin, a prostaglandin synthetase inhibitor, to cultures. Thus it would appear that physical stress causes lymphocytes to become more sensitive to prostaglandin E<sub>2</sub>, and the increased sensitivity to inhibition by this immunomodulator is responsible in part for the depressed cellular immune function after physical stress.

**138. Graafsma, S.J., L.J.H. Van Tits,**

**P.H.G.M. Willems, M.P.C. Hectors,**

**J.F. Rodrigues de Miranda,**

**J.J.H.H.M. De Pont, and Th. Thien:**

β<sub>2</sub>-adrenoceptor up-regulation in relation to cAMP production in human lymphocytes after physical exercise.

*British Journal of Clinical Pharmacology*  
30:142S-144S, 1990.

**Authors' abstract**

The effect of isotonic bicycle exercise on β<sub>2</sub>-adrenoceptors and cAMP production in lymphocytes was studied. The origin of the newly exposed receptors was studied by measuring radioligand binding in the presence of hydrophilic or lipophilic "cold" ligands. During exercise β<sub>2</sub>-adrenoceptor density increased from  $1207 \pm 144$  to  $1776 \pm 152$  sites/cell ( $56 \pm 14\%$ ). Isoprenaline induced an increase in cAMP synthesis, which was  $68 \pm 15\%$  higher than those values measured before the test. Forskolin did not induce a higher increase in cAMP production after exercise. The increase in receptor density seems not to be due to a transfer of internalized receptors to the membrane surface. We conclude that physical exercise induces an up-regulation of β<sub>2</sub>-adrenoceptors on lymphocytes and that these adrenoceptors are functional.



**139. Graubaum, H.-J., Chr. Metzner, and**

**K. Ziesenhenn:**

Körperliche Belastung und hepatitisverlauf.  
*Deutsche Medizinische Wochenschrift* 112:47-49,  
1987.

**Authors' abstract**

Twenty-five patients with clinically and histologically verified acute hepatitis were subjected to a submaximal bicycle ergometer exercise during the first week after inpatient admission and afterwards subdivided into two groups. The first group maintained bedrest, and the other group trained for 30 minutes a day over six weeks at an exercise level amounting to 70% of the submaximal performance of the initial ergometry. Histological, clinical and laboratory results did not differ between the groups. It is concluded that immobilization for a short time only is indicated in acute hepatitis.

**140. Green, R.L., S.S. Kaplan, B.S. Rabin,**

**C.L. Stanitski, and U. Zdzarski:**

Immune function in marathon runners.  
*Annals of Allergy* 47:73-75, 1981.

**Authors' abstract**

Quantitative immunoglobulins (IgG, IgA, IgM) and leukocyte phagocytosis and killing were studied in 20 male marathon runners to determine if rigorous physical conditioning affects immune function. C<sub>3</sub>, C<sub>4</sub>, Properdin Factor B, T and B cells, and phytohemagglutinin and pokeweed mitogen stimulation of lymphocytes were determined in selected runners. Complete blood counts, including platelets, were obtained for the group. Mean immunoglobulin values for IgG, IgA and IgM were within normal limits. Ten runners (50%) had slightly low total lymphocyte counts (less than 1500/mm<sup>3</sup>). Leukocyte phagocytosis and killing was consistently normal. Nine marathoners felt that running had increased, and one felt that it had decreased their resistance to respiratory infections. This could not, however, be correlated with significant changes in immune parameters. We conclude that long distance running has no effect on immune function.

**141. Grimm, V.H.:**

Die Bedeutung des Gamma-Globulins für den Spitzensport.  
*Sportarzt und Sportmedizin* 4:89-92, 1973.

**Synopsis**

The importance of gamma-globulins, in the prophylaxis of viral and bacterial diseases, has been appreciated in the

course of the last years. Excellent results have been achieved with a correct dosage, administered in time. The good experiences gained with gamma-globulins, in the members of the German Olympic team (canoë-slalom) suggest their use on a large scale in competition sportsmen.

**142. Halicka-Ambroziak, H.D., M. Wiktor,**

**A. Smykowska, E. Ciszewska, and**

**J. Roszko:**

Wplyw wysilku fizycznego na opornosc osmotyczna leukocytow. (The effect of physical effort on the osmotic resistance of leukocytes).  
*Wychowanie Fizyczne i Sport* 4:127-131, 1971.

**Authors' abstract**

The effect of physical effort on the osmotic resistance of leukocytes was checked on 20 students of the Physical Education Academy in Warsaw. One group performed work which consisted in stepping on a step 40 cm high at the rate of 22.5 steps per minute over 21 minutes. Another group performed work equal to 900 kgm/min for 10 min on a bicycle ergometer. The index of changes in the osmotic resistance was the proportion of leukocytes preserved in an 0.2% NaCl solution in comparison with the number of white blood corpuscles in Turk liquid, which represented 100%. Peripheral blood spreads were also made. A significant reduction of the osmotic resistance was found in both groups (17.18% in the first group and 13.12% in the second group). The number of young forms of neutrophile leukocytes increased. It is assumed that one of the factors causing the reduction of the osmotic resistance of leukocytes is the increase in the number of young forms of white blood corpuscles whose resistance is weaker than that of multi-lobe forms.

**143. Hansen, J.-B., L. Wilsgard, and**

**B. Østerud:**

Biphasic changes in leukocytes induced by strenuous exercise.  
*European Journal of Applied Physiology* 62:157-161, 1991.

**Authors' abstract**

Seven healthy male volunteers participated in short- (STR, 1.7 km), middle- (MTR, 4.8 km) and long- (LTR, 10.5 km) term runs at a speed close to their maximum. A prompt mobilization of white cells, and lymphocytes in particular, appeared following the exercise. The initial increase in the number of lymphocytes was succeeded by a significant decrease [ $P < 0.03$ ], lymphopenia, which on average was 32%-39% of the pre-exercise values in all

groups. A close correlation was found between the initial increase in plasma cortisol concentration after exercise and the subsequent lymphopenia. A modest enhancement in the number of granulocytes immediately after the exercise was accompanied by a comprehensive increase in polymorphonuclear (PMN) elastase concentration accounting for 78.6%, SEM 16.3%, 140.7%, SEM 31.8% and 241.3%, SEM 48.1% in the STR, MTR, and LTR groups. No correlation was found between granulocyte number and the plasma PMN elastase concentration. A delayed granulocytosis was noted in all subjects, reaching a peak between 2 and 4 hours after the exercise. The magnitude of the granulocytosis varied among subjects and peak values of the number of circulating granulocytes were found to be  $5.7 \times 10^9$  cells $\cdot$ l $^{-1}$ , SEM 0.5,  $6.7 \times 10^9$  cells $\cdot$ l $^{-1}$ , SEM 0.6 and  $8.8 \times 10^9$  cells $\cdot$ l $^{-1}$ , SEM 0.5 in STR, MTR, and LTR, respectively, whereas the mean baseline value was  $3.6 \times 10^9$  cells $\cdot$ l $^{-1}$ , SEM 0.4. The neutrophilic granulocytosis was not accompanied by a corresponding enhancement in PMN elastase concentration. The plasma cortisol concentration reached a peak 30 minutes after exercise and declined below the control level in 4 hours. Neither the initial increase nor the subsequent decrease in plasma cortisol concentration were found to be essential for the magnitude of the delayed leukocytosis.

#### 144. Hanson, P.G. and D.K. Flaherty:

Immunological responses to training in conditioned runners.  
*Clinical Science* 60:225-228, 1981.

##### Authors' abstract

1. We measured the concentrations of leucocyte subpopulations, immunoglobulins and complement in six well-conditioned runners before and after a typical 8-mile (12.8 km) training run at 70-75% of  $\dot{V}O_2$  max.
2. Before running all components were within the normal range. Exercise failed to produce a significant rise in neutrophils. There was also no change in immunoglobulins or complement concentrations immediately or 24 hours after exercise. Lymphocyte subpopulations were also unchanged except for a progressive rise in antibody dependent cytotoxic effector cells (K-lymphocytes).
3. These results suggest chronic exercise training has no apparent adverse effect on circulating cellular or humoral immune components in healthy subjects. An increase in K-lymphocytes may provide added host defense capacity during periods of stress, although the mechanism of increase is unexplained.

#### 145. Hargreaves, E.R.:

Poliomyelitis: Effect of exertion during the pre-paralytic stage.  
*British Medical Journal* 2:1021-1022, 1948.

##### Author's abstract

The effect of physical or mental exertion during the pre-paralytic stage of poliomyelitis on the ultimate prognosis is analysed in thirty cases of the disease which occurred in Cornwall during 1947-8. The findings support those of Russell (1947)—namely that severe physical activity during the pre-paralytic stage is associated with grave prognosis. Severe mental strain, such as driving a car over long distances, appears to be equally disastrous, whereas paralysis tends to be mild in cases confined to bed during the pre-paralytic stage.

#### 146. Harisch, G., E. Szász, G. Amtsberg,

G. Kirpal, H.-P. Sallmann, and J. Schole:  
Resistenzänderung durch Belastung und Ernährung. 1. Mitteilung: Bakterielle Infektion.  
*Zentralblatt für Veterinärmedizin B* 25:729-740, 1978.

##### Authors' abstract

Survival rate and index of phagocytosis have been investigated in male Wistar rats and male mice which had been stressed in different ways and inoculated afterwards with *Salmonellae* or *Pasteurellae*. The following results were obtained:

1. In the case of a single application of the bacterial lipopolysaccharide Vaccineurin® all test rats inoculated with *Salmonellae* or *Pasteurellae* 24 hours later survived. All control animals died. The index of phagocytosis was elevated at 130% compared with control animals. The survival rate of mice increased remarkably.
2. Five times swimming at daily intervals is able to influence survival rate and index of phagocytosis in rats positively. In contrast, 8 or 15 times swimming gives rise to a decrease of resistance.
3. Feeding a fat diet (i.e., isoenergetic replacement of carbohydrates by fat-energy) caused an increase in survival from 15% in carbohydrate controls to more than 70%. The effect depends on the duration of the dietary change. Phagocytosis shows only a moderate increase. The enhancement in resistance is discussed as a functional optimum of the defense system which is brought about by endocrine changes during the stress conditions employed.

**147. Hartmann, G., H. Michna, and W. Schänzer:**

Cardiac and suprarenal mediators of peritoneal macrophage activity and training.  
*International Journal of Sports Medicine* 8:157, 1987.

**Authors' abstract**

The reaction of autonomic nervous tissue and cellular immune system to training load was assessed using the experimental model of treadmill exercise. Female mice were divided into two groups: One group served as controls; the others were subjected to treadmill exercise (one week). The adrenergic portion of the intracardiac nervous system was studied by means of glyoxal acid-induced fluorescence. The area of fluorescent nerve fibers was measured using an image analyzing system; catecholamine concentrations were determined by gas chromatography/mass spectrometry (GC/MS); suprarenal catecholamine concentration was quantified using a high pressure liquid chromatograph with electrochemical detection (HPLC-EC). The assessment of the activity of the cellular immune system is limited to the activity of peritoneal macrophages: phagocytosis, migration in the modified Boyden chamber, chemotaxis in the agarose-migration assay and cytotoxicity against sarcoma cells were tested. The enlarged area of fluorescent nerve fibers and elevated noradrenaline concentration in the ventricular myocardium indicate increased sympathetic activity. These results can be correlated with the macrophages' increased capacity for phagocytosis, migration, and cytotoxicity. The catecholamine concentration in the suprarenal medulla is unchanged at the time of this study. These findings are discussed with regard to a possible functional connection of the activities of macrophages and catecholaminergic systems.

**148. Hedfors, E., P. Biberfeld, and**

**J. Wahren:**

Mobilization to the blood of human non-T and K lymphocytes during physical exercise.  
*Journal of Clinical and Laboratory Immunology* 1:159-162, 1978.

**Authors' abstract**

Highly purified blood lymphocytes from healthy individuals were investigated before and after a standardized bicycle ergometer test through sampling from catheters inserted into the brachial artery and the hepatic vein. The physical activity resulted in an increase of circulating lymphocytes mainly accounted for by an increase of circulating EAC-rosette forming cells

including an increase of K-cells. No differences were found in the proportions of E- and EAC-rosette forming cells at rest or during exercise between samples from arterial or hepatic venous blood, nor were any differences in K-cell cytotoxicity against chicken red blood cells found between arterial and venous samples. The data indicate that physical activity leads to the mobilization of lymphocytes to the blood from non-splenic sites with a change in subpopulation composition and K-cell cytotoxicity.

**149. Hedfors, E., G. Holm, M. Ivansen, and**

**J. Wahren:**

Physiological variation of blood lymphocyte reactivity: T-cell subsets, immunoglobulin production, and mixed-lymphocyte reactivity.  
*Clinical Immunology and Immunopathology* 27:9-14, 1983.

**Authors' abstract**

Highly purified blood lymphocytes from healthy individuals were obtained from samples collected before and after a standardized bicycle ergometer test. In accordance with previous findings physical work resulted in a marked increase of circulating lymphocytes, with a proportionate decrease of T lymphocytes and increase of non-T lymphocytes including B cells. The decrease of T lymphocytes was accounted for by a reduction of cells reactive with the monoclonal OKT4 serum (helper/inducer), whereas the proportion of OKT8-positive cells (suppressor/cytotoxic) remained unchanged. The lymphocyte production of IgG, IgM, and IgA after 7 days culture with pokeweed mitogen and the lymphocyte DNA synthesis after activation by allogenic cells was reduced during work. It is concluded that nonspecific stress changes the composition of T-lymphocyte subsets with depression of T-cell stimulation and T-cell-dependent immunoglobulin production.

**150. Hedfors, E., G. Holm, and B. Öhnell:**

Variations of blood lymphocytes during work studied by cell surface markers, DNA synthesis and cytotoxicity.  
*Clinical and Experimental Immunology* 24:328-335, 1976.

**Authors' abstract**

Highly purified blood lymphocytes from healthy individuals were obtained from samples collected before and after a standardized bicycle ergometer test. The physical activity resulted in a marked increase of circulating lymphocytes. The proportion of T lymphocytes

estimated as cells forming rosettes with sheep red blood cells after incubation in the cold decreased, whereas a corresponding increase of cells with receptors for C3, IgG-Fc or surface immunoglobulin was noted. Moreover, after work an increase of cells simultaneously reacting with cell surface markers usually designed as T- or B-cell markers occurred. The reactivity of lymphocytes collected after work in response to Con A, PHA, PWM and PPD was impaired, whereas the slight response to LPS was unchanged. The K-cell cytotoxicity of lymphocytes collected after work increased. The data indicate that physical activity leads to the mobilization of lymphocytes from as yet undetermined sites and with changed composition and reactivity.

#### 151. Hedin, G. and G. Friman:

Orthostatic reactions and blood volumes after moderate physical activation during acute febrile infections.

*International Rehabilitation Medicine* 4:107-109, 1982.

##### Authors' abstract

In 18 patients suffering from viral, mycoplasma or bacterial infections, orthostatic reaction and total haemoglobin were measured after termination of fever and 1 and 3 months thereafter. The results of the 3 months control were considered to represent the individual's normal values. The patients were randomized into two groups, one of which was subjected to a physical activity programme when febrile and the other, serving as control group, was confined to bed according to traditional clinical routine. The orthostatic reaction was measured as the mean heart rate during 10-min tilting on a tilt table. Plasma and red cell volumes were calculated from total haemoglobin, haemoglobin concentration and erythrocyte volume fraction. After fever heart rate during tilt was, in both groups, significantly higher than at the 3 months' control, but it was lower in the trained group ( $86 \pm 4$  beat/min) than in the control group ( $100 \pm 3$  beats/min) ( $P < 0.05$ ). Plasma volume and red cell volume, both being numerically reduced in our patients after fever, showed a significant increase 3 months after illness only in the untrained control group. The results suggests that physical activity during acute febrile infections prevents the illness/bed rest induced orthostatic deterioration and blood volume reduction.

#### 152. Heilbrunn, L. V., A. Halaban, and W.L. Wilson:

An attempt to influence the survival time of cancerous mice.

*Biology Bulletin* 103:282, 1952.

##### Authors' abstract

Experiments of Most in our laboratory have shown that when muscle is fatigued it gives off heparin or heparin-like substances (Most, 1953). In view of the fact that heparin prevents cell division, and in view of the fact also that Bullough (1948) found that exercise markedly decreased the rate of mitosis in the skin of mice, we investigated the effect of exercise on the survival time of mice implanted with tumors. We used two types of malignant tumors, and the mice with these tumors were placed in cages containing an exercise wheel. The survival time of these mice was compared with the survival time of similar mice in cages without exercise wheels. Exercise appears to have a favorable effect on the survival time.

#### 153. Henschel, A., H.L. Taylor, and A. Keys:

Experimental malaria in man. I. Physical deterioration and recovery.

*Journal of Clinical Investigation* 29:52-59, 1950.

##### Authors' abstract

1. Malaria was induced in 12 normal young men by inoculation with 3 cc of blood infected with the McCoy strain of *Plasmodium vivax*. The malaria was terminated with quinine sulphate after five to eight paroxysms and an average of 193 degree hours of temperature above  $101^{\circ}$  F.
2. Blood hemoglobin concentration was reduced an average of 3.3 g/100cc of blood. Total plasma volume was not changed. Complete recovery of the hemoglobin required about four weeks.
3. The pulse rate during a work test of moderate severity was increased 26.9 beats per minute and recovery rate 29.7 beats per minute on the third post-febrile day; normal values were obtained three weeks after malaria.
4. Maximal oxygen intake was decreased 18.9% on the fifth post-febrile day. About six weeks were required for recovery of the function.
5. Maximal performance capacity as measured by the Harvard Fitness test was depressed until the eighth post-febrile week.
6. Blood lactate concentration was increased 56.2% at standard rest and 101.9% 12 minutes after short exhausting work. Blood pyruvate concentration was

increased 45.9% after the hard work but the resting pyruvate concentration was not increased.

7. Cardiovascular stability as measured by the tilt-table deteriorated about 50% during the malaria but was essentially normal three to four weeks after the malaria.

8. The excretion of 17-ketosteroids was depressed during the experimental malaria.

**154. Hickson, R.C. and J.B. Boone, Jr.:**

Physical exercise and immunity.

In: *Stress and Immunity*, edited by N. Plotnikoff, A. Murgo, R. Faith, and J. Wybran. Boca Raton, FL: CRC Press, 1991. p. 211-234.

**Authors' abstract**

Based on the available evidence, single bouts of exercise may create an immunosuppressive state within the circulation, particularly following long-term exercise. The immunosuppression appears transient and can return to pre-exercise levels within minutes or hours, depending on the study. There is presently no strong evidence to indicate exercise intensity has a key role in either immunosuppression or immunostimulation. Several studies have demonstrated several positive immune responses, and in particular, natural killer activity increases with most durations of exercise reported to date. Additionally, several investigations have reported a delayed immunostimulation following exercise. Several positive immune system effects of endurance training have been demonstrated. They include increased *in vitro* mitogenesis and T-cell formation at rest. Highly trained individuals may also have greater natural killer cell activity. Endurance training can also result in a smaller reduction of certain immunosuppressive responses (i.e., *in vitro* mitogenesis on a parallel basis) to exercise. Another major area of physical activity, strength training, has only begun to receive attention regarding its action on the immune system. Much of this work remains to be completed. Various mechanisms have been proposed to explain the exercise-immune interplay. Catecholamines and glucocorticoids may exert positive and negative effects, respectively, on lymphocyte responsiveness following exercise. Opioids may have a pivotal role in the regulation of natural killer cell activities. However, the number of potential modulators of immune system action suggests a vast participation by a number of compounds. Further in-depth investigations of the specific mechanisms involved in the exercise-related immune responses would appear to represent a wide-open topic for future research. Another area in which exercise may have positive effects is in immunosuppressed individuals. Following this line of reasoning, the absence of

stimulation observed in many of the exercise studies might be attributed to the fact that the normal immune system is already functioning at or near optimal levels. Whether regular exercise training is capable of reversing immunosuppression remains an important unanswered question.

**155. Hirsch, A.:**

Influence de certains facteurs non spécifiques sur la multiplication du bagille tuberculeux dans l'organisme animal. 1. -Effets du travail musculaire sur l'évolution de l'infection tuberculeuse de la souris et du rat.

*Annales de L'institut Pasteur* 109:454-459, 1965.

**Author's abstract**

In 13 experiments, muscular exercise (swimming) did not alter the course of experimental tuberculosis in rats and mice. In one experiment, a slowing down of bacillary growth was observed under well defined conditions. In rats, confinement increases bacillary multiplication in the spleen.

**156. Hirsén, D.J. and L.M. Malham:**

Effect of exercise on cytotoxic lymphocytes. *Federation Proceedings* 42:438, 1983.

**Authors' abstract**

The mobilization of lymphocytes into peripheral blood by exercise was examined in order to test the hypothesis that human natural killing (NK) and antibody dependent cell mediated cytotoxicity (ADCC) are mediated by the same lymphocytes. Peripheral blood mononuclear cells (PBM) were obtained from 7 volunteers prior to treadmill exercise (baseline) and at 0, 7.5, 15, and 30 minutes post exercise. They were tested in  $^{51}\text{Cr}$  release assays of NK of k562 erythroleukemia cells and ADCC of Chang liver cells. The proportional increases over baseline were determined at each post-exercise time for total PBM per  $\text{mm}^3$  whole blood and cytotoxic lytic units per  $10^6$  PBM giving 50%  $^{51}\text{Cr}$  release. Immediately post-exercise, total PBM were increased by  $1.7 \pm 0.1$ , NK by  $5.1 \pm 0.7$  and ADCC by  $5.4 \pm 0.9$  ( $\bar{X} \pm \text{S.E.}$ ), indicating that NK and ADCC effector cells were mobilized in greater proportions than total PBM. Total PBM counts returned to baseline levels at 7.54 minutes post-exercise, at which time NK and ADCC were still increased by  $3.1 \pm 0.3$  and  $2.8 \pm 0.3$ , respectively. The proportional increases were similar for NK and ADCC at each post-exercise time in all 7 experiments, and the values returned to baseline simultaneously at 30 minutes post-exercise. The data suggest that NK and ADCC effector cells move

into and out of the circulation in the same numbers over time and independently of other lymphocytes. This supports the hypothesis that NK and ADCC are mediated by the same lymphocytes.

**157. Hoffman, S., K.E. Paschkis, and**

**A. Cantarow:**

Exercise, fatigue and tumor growth.

*Federation Proceedings* 19:396, 1960.

**Authors' abstract**

There is but scant information on the effects of vigorous exercise on tumor growth. In the experiments reported in the literature the effects were considered and discussed from the angle of effects of "stress" on tumor growth. Reports on the effects of extracts of fatigued muscles on growth of tetrahymena suggest a more specific effect of muscular exercise. In our experiments the growth of Walker 256 in rats vigorously exercised was compared with that of controls who were individually housed in small cages permitting them only a minimum of movements. In all instances the weight of the tumors of the controls exceeded considerably and significantly that of exercised animals; no difference in carcass weight was observed between the two groups. Subsequently excised rat muscles were suspended in saline solution and electrically stimulated to "fatigue" evidenced by cessation of contraction upon stimulation. Injection into tumor bearing rats of a preparation made of bathing fluid of a fatigued muscle markedly inhibited tumor growth, whereas a similar preparation from non-fatigued muscle was ineffective.

**158. Hoffman, S.A., K.E. Paschkis,**

**D.A. DeBias, A. Cantarow, and**

**T.L. Williams:**

The influence of exercise on the growth of transplanted rat tumors.

*Cancer Research* 22:597-599, 1962.

**Authors' abstract**

Growth of the Walker 256 tumor in vigorously exercised male Wistar rats was compared with that of control animals confined in small, individual cages, permitting a minimum of movement. In each instance the weight of the tumor in the control group significantly exceeded that in the exercised group. In several instances there was complete tumor regression in the exercised animals. Rat muscles were suspended in a 0.85% NaCl bath and electrically stimulated to "fatigue." An extract of this bath (F-substance) inhibited the growth of the Walker 256 and Murphy lymphosarcoma when injected either at the tumor

site or on the opposite side. An extract prepared in a similar manner from non-fatigued muscle was found to be ineffective.

**159. Hoffman-Goetz, L., R. Keir, R. Thorne, M.E. Houston, and C. Young:**

Chronic exercise stress in mice depresses splenic

T lymphocyte mitogenesis *in vitro*.

*Clinical and Experimental Immunology* 66:551-557, 1986.

**Authors' abstract**

This study investigated changes in functional response to splenic T lymphocytes of mitogens following acute and chronic exposure to endurance exercise. Splenic T cell response *in vitro* to concanavalin A (Con A) and the total number of lymphocytes per spleen were compared between mice assigned to the following treatment conditions: (a) exercise training (EX) by treadmill running (28 m/min, 8° slope for 30 min, 5 times per week for 4 weeks preceded by 2 weeks of endurance build-up), (b) exercise training as above followed by a single acute bout of exercise to exhaustion (EX + AC) (35 m/min, 8° slope, 30 min to 2 h duration) (c) exposure to the novel environment for 6 weeks without exercise (control), and (d) exposure to the novel environment as in (c) followed by a single, acute bout of exercise to exhaustion.

Treadmill running for 6 weeks significantly enhanced succinate dehydrogenase activity in skeletal muscle compared to the sedentary, control condition, and was broadly interpreted as indicative of a training effect. EX mice had significantly reduced splenic lymphocyte proliferative responses to optimal and supraoptimal concentrations of Con A compared with control animals. Incorporation of [<sup>3</sup>H]thymidine into splenic lymphocytes from EX + AC mice was the most markedly depressed. Total number of lymphocytes per spleen was significantly lower in EX compared with control mice. These results suggest that chronic exercise challenge in mice is associated with T lymphocyte hyporesponsiveness in the secondary lymphoid organs, such as the spleen.

**160. Hoffman-Goetz, L., J.R. Simpson,**

**N. Cipp, Y. Arumugam, and**

**M.E. Houston:**

Lymphocyte subset responses to repeated submaximal exercise in men.

*Journal of Applied Physiology* 68:1069-1074, 1990.

**Authors' abstract**

The effects of repeated bouts of submaximal cycle ergometry exercise on changes in the percentage of

peripheral blood T-lymphocytes, the T-helper/inducer and T-cytotoxic/suppressor subsets, and natural killer (NK) cells were studied in 18 healthy young men who had no history of regular exercise training. Subjects were matched on the basis of maximal O<sub>2</sub> uptake and assigned randomly to exercise or control groups, with controls resting quietly during the exercise sessions. The percentages of peripheral blood mononuclear leukocytes that reacted with monoclonal antibodies specific for T-lymphocytes (CD3<sup>+</sup> cells), the helper/inducer subset (CD4<sup>+</sup> cells) of T-lymphocytes, and cytotoxic/suppressor subset (CD8<sup>+</sup> cells) of T-lymphocytes, and cells with NK activity (Leu7<sup>+</sup> cells) were enumerated by fluorescence-activated flow cytometry for samples obtained immediately before and after exercise on days 1, 3, and 5 of a 5-day exercise regimen. The results of this study were mixed with decreases in the percentages of T-lymphocytes before vs. after exercise on days 1 and 3 ( $P < 0.001$ ), a decrease in the percentage of T-helper/inducer cells before vs after exercise on day 3 ( $P < 0.05$ ), no effect of exercise on the percentages of T-cytotoxic/suppressor cells, and a marked increase in the percentage of NK cells after exercise on days 1 ( $P < 0.05$ ) and 3 ( $P < 0.01$ ). The total number of recovered NK cells in the mononuclear leukocyte fraction of blood also increased significantly after exercise on days 1 ( $P < 0.05$ ) and 3 ( $P < 0.01$ ). These findings 1) suggest that repeated exposure to submaximal exercise results in consistent increases in the percentage of NK cells, 2) demonstrate that the exercise effects on T-lymphocyte subset percents were variable over time, 3) confirm earlier reports on the impact of a single bout of submaximal exercise on percent and numerical shifts in peripheral blood T-lymphocytes and NK cells, and 4) extend the findings of earlier studies to include individuals of low fitness levels.

#### 161. Hoffman-Goetz, L., R.J. Thorne, and M.E. Houston:

Splenic immune responses following treadmill exercise in mice.

*Canadian Journal of Physiology and Pharmacology* 66:1415-1419, 1988.

##### Authors' abstract

The *in vitro* proliferation response to lipopolysaccharide and pokeweed mitogen by splenic lymphocytes and the effect on the total splenic lymphocyte number were examined in C57BL/6J mice following an 8-week treadmill training program (30 m/min, 8° slope, 30 min/day, 5 times/week) and after a single bout of exhaustive exercise (50% stepwise increases in final running speed for 10 min intervals). Plasma cortico-

sterone levels were also measured to evaluate whether changes in adrenocortical activation were associated with exercise-induced immunomodulation. In comparison to sedentary controls, trained mice had an increase of 35% in succinate dehydrogenase activity per unit of protein in the quadriceps femoris muscle. Trained mice showed an increase in splenic lymphocyte proliferation to both mitogens which was evident 72 h after completion of the final training session, relative to sedentary controls. Immediately following exercise, however, lymphocyte proliferative responses were depressed compared with the training and the control values. The exercise regimen resulted in a reduction in total number of mononuclear cells per spleen. Changes in plasma corticosterone levels after exercise were not clearly associated with immunodepression or immunoenhancement of splenic lymphocyte mitogenesis. Taken together, the data suggest that moderate endurance training augments splenic B lymphocyte mitogenesis and further, that the immediate effects of exercise on splenic immune function vary with the duration and intensity of the work.

#### 162. Hoffman-Goetz, L., R. Thorne,

J.A.R. Simpson, and Y. Arumugam:

Exercise stress alters murine lymphocyte subset distribution in spleen, lymph nodes and thymus.

*Clinical and Experimental Immunology* 76:307-310, 1989.

##### Authors' abstract

Our previous work indicated that exercise stress in mice was associated with reduced splenic lymphocyte proliferation to T cell mitogens. The purpose of this study was to determine the effect of acute exercise stress and exercise training on the phenotype distribution of murine lymphocytes in the spleen, lymph nodes and thymus. In mice given an exhaustive bout of treadmill exercise, the percentage of Thy1.2 and Lyt2 antigen bearing cells decreased in the thymus, but percentages of L3T4-positive cells did not change significantly. Acute exercise did not alter the percentage of Thy1.2, L3T4, or Lyt2-positive cells in the secondary lymphoid compartments (nodes, spleen). By contrast, in mice given a chronic exercise training programme (8 weeks duration; 30 m/min, 8° slope, 30 min/session, 5 daily sessions/week) followed by a 72 h rest period, the percentage of L3T4-positive cells increased by 52% in the spleen, 19% in the lymph nodes, and 29% in the thymus compared with sedentary controls; no parallel increase in the percentage of Thy1.2 antigen bearing cells was observed. These results suggest that the effect of exercise on the frequencies of lymphocyte subpopulations in murine lymphoid compartments is dependent upon the chronicity

of the stress and probably on the accompanying physiological adaptations to stress.

**163. Horstmann, D.M.:**

Acute poliomyelitis. Relation of physical activity at the time of onset to the course of the disease.  
*Journal of the American Medical Association*  
142:236-241, 1950.

**Synopsis**

**Purpose** To study the relation of physical activity at the time of the onset to the course of acute poliomyelitis.

**Methods**

1. 411 patients with poliomyelitis from 3 epidemics (one in North Carolina, Los Angeles County and New York City) were studied to determine the amount of physical activity they performed 3 days before and 3 days after the onset of their illness.
2. Complete clinical histories were obtained and, in those with 2 distinct phases to their illness, activity histories were taken for 3 days prior to the onset of the first phase and 3 days following its onset. History of trauma or unusual physical exertion was noted.
3. The degree of physical activity was noted and data were analyzed according to age, type of disease, and severity of paralysis. Bulbar cases were considered separately.
4. Data were analyzed in various stages of the disease.

**Results**

1. Physical activity performed at the time of the first phase or prior to the onset of the second phase was not associated with an increase in the subsequent development or the severity of paralysis.
2. Physical activity performed after the second phase or major illness was associated with a significant increase in the incidence and severity of subsequent paralysis.
3. A higher percentage of nonparalytic than paralytic patients gave a history of bed rest or minimal activity during the early stages of the major illness.

**Conclusions**

1. The best time for physical activity seemed to be the first 24 to 48 hours of the illness when the symptoms were mild.

**164. Housh, T.J., G.O. Johnson, D.J. Housh, S.L. Evans, and G.D. Tharp:**

The effect of exercise at various temperatures on salivary levels of immunoglobulin A.  
*International Journal of Sports Medicine*  
12:498-500, 1991.

**Authors' abstract**

The purpose of this investigation was to determine the effect of ambient temperature on the salivary immunoglobulin A (s-IgA) response to submaximal exercise. Nine adult males ( $\bar{X}$  age  $\pm$  SD =  $22 \pm 2$  yr) volunteered to perform an incremental treadmill test to exhaustion for the determination of  $\dot{V}O_2$  max and three 30-minute treadmill runs at 80%  $\dot{V}O_2$  max in an environmental chamber at temperatures of approximately 6, 19 and 34°C. Saliva samples were collected prior to each submaximal workout as well as immediately and 1 hr post-exercise. A two-within subjects factors (temperature, sample time) repeated measures ANOVA indicated no significant interaction or main effects for sampling time or temperature. The results of this study indicated that 30 minutes of non-competitive exercise at temperatures ranging from 6 to 34°C had no effect on s-IgA. These findings suggest that moderate intensity exercises at a wide range of ambient temperatures does not increase the susceptibility to upper respiratory infection by decreasing s-IgA.

**165. Houston, H.A.:**

The effect of acute and chronic exercise on immune function in man.

*Masters Thesis:* University of Waterloo, Canada: 1987. 164 p.

**Author's abstract**

This study investigated the effect of acute exhaustive exercise and endurance training on *in vitro* lymphocyte proliferative response to mitogens in adult men. Two groups of subjects (cohort 1, n = 8; cohort 2, n = 8) participated in an eight week endurance cycling program (40 one hour sessions at 70% of  $\dot{V}O_2$  max). Blood samples for immunological and hormonal assessment were obtained from resting, fasted subjects following 72-hours of inactivity, prior to (pre) and following (post) training. Subjects performed acute exhaustive exercise tests at an intensity of 85% initial  $\dot{V}O_2$  max prior to, at the mid point and upon completion of training. Blood samples for immunological and hormonal assessment were obtained from resting subjects immediately before and 30 minutes after exercise. The plasma concentrations of norepinephrine (NE), epinephrine (E), and cortisol were measured at all blood sampling time points. There



was a significant training effect as indicated by increased  $\dot{V}O_2$  max values, endurance test times and reduced heart rates during submaximal exercise. However, cohort 1 had a consistently greater training response than cohort 2. All subjects showed significantly decreased body weight and fat percentage following training. Lymphocyte proliferative responses to T- and B-cell mitogens were either unchanged or depressed from pre- to post-training, which was dependent upon the type and concentration of the mitogen and on the specific cohort. The concentrations of NE, E and cortisol were unchanged as a result of training. Acute exhaustive exercise in untrained subjects either enhanced or did not change the T and B lymphocyte proliferative responses. This was also dependent upon the type and concentration of the mitogen and the specific cohort. The concentrations of NE and cortisol were increased while E levels were unchanged from before to after exercise. Acute exhaustive exercise in trained subjects revealed no change in the lymphocyte proliferation responses to the T-cell and B-cell mitogen. However, lymphocyte proliferative responses determined before the exercise tests were reduced from pre- to post-training. These results suggest that moderate endurance training may be a form of chronic stress that is associated with a depressed or an unchanged lymphocyte dependent immune reactivity. In addition, acute exhaustive exercise is associated with an enhanced or unchanged immune response and endurance training modifies this effect. The hormones NE, E and cortisol do not appear to be associated with the exercise or training-induced changes in the immune system. The biological significance of changes in the immune response and their mechanisms remain to be elucidated.

#### 166. Houston, H., L. Hoffman-Goetz, M.E. Houston, and R. Keir:

Immunological responses to exercise training in man. *Federation Proceedings* 46:680, 1987.

##### Authors' abstract

To test the belief that regularly performed endurance exercise improves disease resistance by enhancing immune function, several *in vitro* parameters of lymphocyte functional responses to mitogens were determined in fasting venous blood in 8 sedentary males 72 h before and after an 8-week endurance cycling program (40 one-hour sessions at 70% of  $\dot{V}O_2$  max). Lymphocyte functional responses were determined by proliferation and incorporation of [ $^3$ H]TdR following a 74 h exposure to optimal concentrations of Con A (5 $\mu$ g/ml), PHA (15 $\mu$ g/ml) and LPS (40 $\mu$ g/ml). The endurance training program resulted in a 3-fold increase in endurance time ( $P < 0.007$ ) and a 17% increase in

$\dot{V}O_2$  max ( $P < 0.0001$ ). Lymphocyte proliferation responses to T-cell mitogens Con A and PHA were depressed after training compared to pre-training (Con A: 27,868  $\pm$  4,888 post vs. 49,217  $\pm$  3,518 pre cpm,  $P < 0.004$ ; PHA: 66,504  $\pm$  6,614 post vs. 80,560  $\pm$  3,033 pre,  $P < 0.02$ ). There were no significant differences pre- compared to post-training for either RPMI-1640 (unstimulated) or LPS (B cell mitogen) proliferation responses. These data suggest that exercise training may be a form of chronic stress associated with a depression in T-lymphocyte dependent immune reactivity. The biological significance of these changes and their mechanisms remain to be elucidated.

#### 167. Howlett, T.A., S. Tomlin, L. Ngahfoong, L.H. Rees, B.A. Bullen, G.S. Skrinar, and J.W. McArthur:

Release of  $\beta$  endorphin and met-enkephalin during exercise in normal women: response to training. *British Medical Journal* 288:1950-1952, 1984.

##### Authors' abstract

Plasma  $\beta$  endorphin and met-enkephalin concentrations were measured in response to treadmill exercise in 15 normal women before, during, and after an intensive program of exercise training. Significant release of  $\beta$  endorphin occurred in all three test runs, and the pattern and amount of release were not altered by training. Before training dramatic release of met-enkephalin was observed in seven subjects and smaller rises observed in a further four, and this response was almost abolished by training. This represents the first observed "physiological" stimulus to met-enkephalin release. Endogenous opioid peptides play a part in adaptive changes to exercise training and probably contribute to the menstrual disturbances of women athletes.

#### 168. Ilbäck, N.-G., D.J. Crawford, H.A. Neufeld, and G. Friman:

Does exercise stress alter susceptibility to bacterial infections? *Upsala Journal of Medical Sciences* 96:63-68, 1991.

##### Authors' abstract

Swimming was used for evaluating alterations in performance capacity as a means for studying the influence of exercise stress on susceptibility to *Streptococcus pneumoniae* and *Francisella tularensis* infections in two strains of rats, i.e. Fisher-Dunning (FD) and Sprague-Dawley (SD). The performance capacity was reduced by both diseases and was correlated to the dose of the given micro-organism. FD rats, however, were

more susceptible to the infection and showed a greater deterioration than SD rats. The effects of exercise stress on disease lethality varied with the time that it was performed. Strenuous exercise immediately before infection drastically reduced susceptibility to either of the bacteria, while a similar bout of exercise performed after infection increased disease-related mortality in both diseases.

**169. Ilbäck, N.-G., J. Fohlman, and**

**G. Friman:**

Exercise in coxsackie B3 myocarditis: Effects on heart lymphocyte subpopulations and the inflammatory reaction.

*American Heart Journal* 117:1298-1302, 1989.

**Authors' abstract**

To investigate whether exercise in coxsackie B3 virus infection is detrimental to the myocardium, Balb/c mice were inoculated with the virus and exercised to exhaustion on a motor-driven treadmill up to 48 hours after the inoculation. This infection evokes myocarditis. The inflammatory and necrotic lesions in the ventricular myocardium 7 days after inoculation covered 4.32% of the tissue section area in the nonexercised group. Exercise at 0 hours did not affect this myocardial damage (4.77%), whereas exercise at 48 hours after the inoculation increased the lesion to 7.85% ( $P < 0.05$ ). Lethality was not influenced by exercise. The response pattern of myocardial lymphocyte subpopulations was studied with an immune histochemical staining technique. The number of T cytotoxic, T suppressor cells increased threefold ( $P < 0.01$ ) with exercise at 48 hours but was unchanged with exercise at 0 hours. The number of class II expressing cells decreased with exercise at 48 hours ( $P < 0.05$ ) and was negatively correlated ( $P < 0.01$ ) with the size of the inflammatory reaction. The development of myocardial inflammatory and necrotic lesions seems to be dependent on the presence and cooperation of class II expressing cells and T killer cells. Furthermore, failure to restrict physical activity in the acute phase of this infection may well contribute to the progression of the disease.

**170. Ilbäck, N.-G., G. Friman, and**

**W.R. Beisel:**

Response of the mouse myocardium to physical exercise during infection with *F. tularensis* or influenza and modifying effects of physical preconditioning.

*Clinical Research* 30:369A, 1982.

**Authors' abstract**

In an effort to compare the effects on the myocardium of forced exercise (daily swimming to exhaustion) in the acute phase of a bacterial infection to those in a viral infection, and to determine if physical preconditioning (daily swimming for 6 weeks prior to inoculation) was beneficial, *F. tularensis* (Ft) and influenza (I) infections of similar intensity were used in mouse models.

Two days before median lethality was achieved, lactate dehydrogenase, citrate synthase, cytochrome c oxidase, cathespins D,  $\beta$ -glucuronidase, protein, RNA, and DNA were determined in whole heart homogenates. Both infections caused expected catabolic alterations in resting, unconditioned control mice (a more pronounced decrease of glycolytic and oxidative enzyme activities, protein and RNA in I than in Ft infection). In both infections, preconditioning limited infection-induced catabolic responses. Forced exercise during Ft infection in unconditioned mice reduced the infection-induced decrease in the activities of glycolytic and oxidative enzymes, but lethality was uninfluenced. Conversely, forced exercise in the I infection increased lethality and had no protective effect on biochemical parameters observed. The activation of cathespins D and  $\beta$ -glucuronidase was mainly infection-induced. Thus, preconditioning limited the catabolic effects caused by both infections. Further, forced exercise in Ft infection in unconditioned mice evoked a training response that partly counteracted the degradation caused by the infection, whereas, in the I infection, protein degradation was not prevented by exercise and lethality increased.

**171. Ilbäck, N.-G., G. Friman, W.R. Beisel,**

**A.J. Johnson, and R.F. Berendt:**

Modifying effects of exercise on clinical course and biochemical response of the myocardium in influenza and tularemia in mice.

*Infection and Immunity* 45:498-504, 1984.

**Authors' abstract**

For a study of the interactions of strenuous physical exercise (daily swimming to exhaustion) and a viral as compared with a bacterial infection with regard to the clinical course and the biochemical response of the

myocardium, influenza and tularemia of similar lethality were used in mice. In both infections, expected infection-induced catabolic alterations in the ventricular myocardium were evident 2 days before median lethality was achieved, with a more pronounced wasting in influenza than in tularemia. Exercise before inoculation (pre-conditioning) was beneficial in that the catabolic effects of both infections were limited and lethality of influenza was reduced. Thus, the myocardial protein-degrading effect of influenza did not occur with pre-conditioning, and oxidative tissue enzyme activities decreased less. In tularemia, cytochrome c oxidase activity was fully preserved with pre-conditioning, and activation of catalase was less pronounced. Exercise during ongoing infection counteracted the infection-induced decrease in the activities of glycolytic and oxidative enzymes in tularemia, but lethality and bacterial counts in the spleen were uninfluenced. Conversely, exhaustive exercises with influenza increased lethality and had no significant effect on cardiac enzymes. These exercise models caused no major alterations in activation of lysosomal enzymes ( $\beta$ -glucuronidase and cathepsin D).

#### 172. Ilbäck, N.-G., G. Friman,

**D.J. Crawford, and H.A. Neufeld:**

Effects of training on metabolic responses and performance capacity in *Streptococcus pneumoniae* infected rats.

Medicine and Science in Sports and Exercise  
23:422-427, 1991.

##### Authors' abstract

These experiments were designed to study whether endurance training prior to *Streptococcus pneumoniae* infection in rats ( $N = 15$  in each group) alters lethality, performance capacity, and related energy metabolism. A 5-d-wk<sup>-1</sup>, 4-wk-long pre-infection training program with gradually increasing swim time caused no protection from lethality (48% at 72 h post-inoculation), but performance capacity increased by 68% ( $P < 0.01$ ). The catabolic responses as evidenced by changes in insulin and glucagon levels were less pronounced. Mobilization of free fatty acids increased twofold ( $P < 0.01$ ), and improved ketonemic adaptation (47%,  $P < 0.01$ ) occurred with concomitant saved carcass, liver, and skeletal muscle glycogen contents ( $P < 0.01$ ). This shift from carbohydrate toward fat metabolism during exercise as a result of training was also reflected by 21% lower ( $P < 0.01$ ) blood lactate levels. It was concluded that the improved metabolic status, characterizing the trained as compared with the untrained host, is partly preserved during ongoing acute gram-positive bacterial infection.

#### 173. Ilbäck, N.-G., G. Friman, R.L. Squibb, A.J. Johnson, D.A. Balentine, and

**W.R. Beisel:**

The effect of exercise and fasting on the myocardial protein and lipid metabolism in experimental bacterial myocarditis.

*Acta Pathologica, Microbiologica et Immunologica Scandinavica A* 92:195-204, 1984.

##### Authors' abstract

A generally nonlethal *Salmonella typhimurium* infection in weanling rats produced bacterial myocarditis and myocardial hyperplasia. Myocardial lesions were characterized by focal infiltrates of inflammatory cells (predominantly mononuclear), segmental bacterial necrosis, and incipient fibrosis. Although bacterial infections are infrequently associated with myocarditis, the *S. typhimurium* infection in young rats produced a new experimental model of diffuse myocardial inflammatory foci. Biochemical changes in the myocardium included great increases in total myocardial contents of protein (23%), RNA (39%) and DNA (43%) and several lipid fractions (35-55%) as well as in tissue activities of acid hydrolases, such as cathepsin D (124%) and  $\beta$ -glucuronidase (135%), all of which contrasted with the relatively limited areas of histologic involvement (1.5%). To study the effects of additional stress in this model infection, some rats were exercised by forced running in wheels for 2 hours and others were fasted for 24 hours before samples were obtained. The short period of forced exercise in this infection caused an additional increase of myocardial protein content (47%) but with no additional change in histology. The expected fasting-induced degradation of protein as well as an infection-associated increase in myocardial lipids were each prevented when rats were fasted during ongoing acute infection. Protein degradation, as reflected by heightened acid hydrolase activities, seemed to occur at a similar rate regardless of other stresses, whereas the rate of myocardial protein synthesis appeared to be alterable.

#### 174. Isaacs, R. and B. Gordon:

The effect of exercise on the distribution of corpuscles in the blood stream.

*American Journal of Physiology* 71:106-111, 1924.

##### Synopsis

**Purpose** To study the effect of violent, prolonged exercise on the blood corpuscles of humans.

### Methods

1. 17 male marathon runners ran a 26.25-mile race in 2.5 and 3 hours.
2. Blood was taken from the ear capillaries directly before and soon after the race.
3. Differential counts of white blood cells were made.

### Results

1. All individuals showed a relative and absolute increase in the number of polymorphonuclear neutrophil leukocytes and blood platelets in the peripheral circulation.
2. The character of the red cells and the relative percentages of immature forms remained practically unchanged in the peripheral circulation.
3. There was no definite evidence of newly formed or immature cellular elements (with the possible exception of the blood platelets) being added to the circulation.
4. An increased number of young red cells and, in some cases, blood platelets and white cells, in the blood was observed before the race.

### Conclusions

1. The change in the number of white cells and blood platelets is probably the result of a more thorough mixing of the blood of the internal and peripheral blood vessels, with a redistribution of its elements.
2. The above results suggest a possible relationship between the previous period of training and the slightly lowered threshold of blood cell delivery.

### 175. Ivanova, N.I., and V.V. Talko:

The effect of physical loads on the immune systems.  
*Teoriya i Praktika Fizicheskoi Kultury* 1:24, 1981.

#### Authors' abstract

We conducted a comparative evaluation of the T and B immune systems and the degree of phagocytosis in order to determine the most labile links in the immune system. To do this we established sensitive and informative tests which would indicate the condition of the immune system under varying physical loads. The results show that a single maximum physical load (rabbits running on a treadmill until they reach total exhaustion) causes significant changes in the immune system: there is a sharp drop in the reaction of blast transformation of T-lymphocytes in the FGA and the spontaneous migration of leucocytes induced by agar ( $p < 0.001$ ). Platelet-forming cells in the blood increase ( $p < 0.001$ ), which indicates a disruption of immunological homeostasis. The phagocytic activity of neutrophils is depressed to a small

degree: the number of phagocytic cells does not change, but their absorption and digestive capacities decrease ( $3.50 \pm 0.15$ ;  $2.93 \pm 0.16$ ;  $77.5 \pm 2.7$ ;  $66.0 \pm 2.4$ , respectively;  $p < 0.05$ ). The restoration period for

immunological competence exceeds 7 days. Training with physical loads of medium intensity (50% of maximum) causes an increase in a number of factors of the immune system activity. The reactions of blast transformation of T-lymphocytes and spontaneous migration of leucocytes induced by agar are almost double ( $p < 0.01$ ) the values given in the original data. We stimulated an immune response to sheep erythrocytes. The number of antibody-producing cells in the spleen and the titer of antibodies was significantly higher than in healthy animals. The phagocytic reaction of neutrophils was also activated, but to a lesser degree, and only in terms of absorption and digestion of B mesenteriens. The number of phagocytic cells did not increase. On the basis of this research, we can conclude that the T and B immune systems are most sensitive to changes in physical loads. Therefore, it is advisable to include the functional condition of the T and B immune systems when evaluating the effectiveness of physical workouts for preventive and rehabilitative purposes. It should also be taken into consideration when the status of an athlete's immune system is being determined during regular medical examinations.

### 176. Kanonchhoff, A.D., D.J. Cavanaugh,

V.L. Mehl, R.L. Bartels, G.M. Penn, and  
J.A. Budd:

Changes in lymphocyte subpopulations during acute exercise.

*Medicine and Science in Sports and Exercise* 16:175, 1984.

#### Authors' abstract

The purpose of this study was to determine what changes occur in peripheral blood lymphocytes in relation to an acute exercise bout. Eight women, aged 48 to 62, gave informed consent to run on a maximal treadmill until they reached 85% of their predicted maximum capacity as determined by the Karvonen method. Blood samples were drawn from an antecubital vein immediately prior (PRE) and after (POST) exercise. These samples were analyzed for white blood count (WBC); differential lymphocyte count (%LYM); absolute lymphocyte count (ALYM); and the percentages of lymphocyte recovery (REC); B-lymphocytes (B); total lymphocytes; helper T-lymphocytes (HT), and suppressor T-lymphocytes (ST). Also, the ratio of HT to ST (RATIO) was determined. Mean values were analyzed using the two-tailed paired t-test, with a 0.05 level of significance. Means and standard deviations are shown below.

	<u>WBC</u>	<u>%LYM</u>	<u>ALYM</u>	<u>REC</u>	<u>B</u>	<u>AET</u>	<u>HT</u>	<u>ST</u>	<u>RATIO</u>
PRE	5.8	29.8	1.7	57.4	14.1	84.0	51.9	22.8	2.4
± SD	<u>0.7</u>	<u>6.2</u>	<u>0.4</u>	<u>10.2</u>	<u>2.1</u>	<u>3.7</u>	<u>5.2</u>	<u>5.1</u>	<u>0.7</u>
POST	7.8*	37.6*	3.0*	53.3	13.3	83.3	47.8*	25.9	1.9
± SD	<u>1.0</u>	<u>2.5</u>	<u>0.2</u>	<u>7.8</u>	<u>3.7</u>	<u>3.8</u>	<u>6.5</u>	<u>7.3</u>	<u>0.5</u>

Units: WBC and ALYM  $\times 10^3/\text{mm}^3$ .

\*indicates significant difference between PRE and POST means.

These data indicate that an increase in absolute lymphocytes occurs with acute exercise. The only statistically significant change in the lymphocyte subpopulations measured occurs as a decrease in the percentages of HT. The ratio is not different and falls within the normal range of 1.2 to 2.8. Because of this, the statistical decrease in percentage of HT is probably not physiologically significant.

proportion of monocytes (CD14+ cells) 2 hours after exercise and epinephrine infusion, we suggest that, after stress, prostaglandins released by monocytes are responsible for down regulation of NK cell function. Our findings support the hypothesis that increased plasma epinephrine during physical stress causes a redistribution of mononuclear subpopulations that result in altered function of NK cells.

**177. Kappel, M., N. Tvede, H. Galbo, P.M. Haahr, M. Kjaer, M. Linstow, K. Klarlund, and B.K. Pedersen:**

Evidence that the effect of physical exercise on NK cell activity is mediated by epinephrine.  
*Journal of Applied Physiology* 70:2530-2534, 1991.

#### Authors' abstract

The present study was designed to test the hypothesis that the changes in natural killer (NK) cell activity in response to physical exercise were mediated by increased epinephrine concentrations. Eight healthy volunteers 1) exercised on a bicycle ergometer (60 min, 75% of maximal  $\text{O}_2$  uptake) and 2) on a later day were given epinephrine as an intravenous infusion to obtain plasma epinephrine concentrations comparable with those seen during exercise. Blood samples were collected in the basal state, during the last minutes of exercise or epinephrine infusion, and 2 hours later. The NK cell activity (lysis/fixed number of mononuclear cells) increased during exercise and epinephrine infusion and dropped below basal levels 2 hours afterward. The increased NK cell activity during exercise and the epinephrine infusion resulted from an increased concentration of NK (CD16+) cells in the peripheral blood. On the other hand, the decreased NK cell activity demonstrated 2 hours after exercise and epinephrine infusion did not simply reflect preferential removal of NK cells from the blood, because the proportion of CD16+ cells was normalized. On the basis of the finding that indomethacin abolished the suppressed NK cell activity *in vitro* and the demonstration of a twofold increase in the

**178. Karpova, J.I., E.N. Mokhova, and N.I. Volkov:**

The effect of mitochondrial energetics inhibitors on spontaneous rosette formation of lymphocytes from athletes.  
*Journal of Sports Medicine* 22:165-171, 1987.

#### Synopsis

**Purpose** To study the effect of cellular respiration on oxidative phosphorylation inhibitors, as well as uncouplers, on SRF of lymphocytes from athletes after recovery and physical stress.

#### Methods

1. Finger blood samples were taken from cyclists, track-and-field athletes, skaters, swimmers, and hockey players in recovery from competition, and from cycle ergometer exercise.
2. The maximal test on the ergometer involved increasing the load by 450 kg-m/min each 2 min.
3. Blood was analyzed for T-lymphocytes and spontaneous rosette formation.

#### Results

1. Inhibitors of cellular respiration (Rotenone, NaCn), oxidative phosphorylation (Oligomycin), and uncouplers suppress spontaneous rosette formation of lymphocytes with sheep's red cells (SRC), the effect being dependent on the functional state of the test subject.
2. After recovery these inhibitors increase the percentage of lymphocytes which do not bind SRC and decrease the

percentage of lymphocytes with 3 or more and 7 or more SRC in the rosettes.

3. After 3-6 minutes of strenuous bicycle exercise, which has no strong effect on rosette formation per se, the effect of the inhibitors decreases and does not exceed 20-30% during the recovery period when the inhibitor effect further decreases.

4. Cellular respiration inhibitors and mitochondrial ATP-ases as well as uncouplers, effect 1.5-2-fold changes in SRF indices upon complete recuperation.

#### *Conclusion.*

1. The effect of mitochondrial energetics inhibitors on SRF depends on the state of the test subject.

### **179. Karpovich, P.V.:**

The effect of basketball, wrestling, and swimming upon white blood corpuscles.

*Research Quarterly* 6:42-48, 1935.

#### *Synopsis*

*Purpose* To study the effects on the differential count on white blood corpuscles produced by basketball, wrestling, and swimming.

#### *Methods*

30 athletes were tested.

For basketball:

1. During intercollegiate and campus competition, blood samples were taken from players. The time of participation varied between eight and twenty minutes and most players were well-trained varsity men.

For wrestling:

1. Varsity wrestlers had blood samples taken during intercollegiate competition. The time of participation varied between 2 minutes 10 seconds and ten minutes.

For swimming:

1. Varsity swimmers had blood samples taken during trials.

#### *Results*

1. In basketball players, there was an increase in neutrophils and monocytes, but no regularity was noticed in the reaction of eosinophils or basophils.

2. Short periods of wrestling produced an increase in lymphocytes (up to 55%), while long periods resulted in an increase of neutrophils (up to 78%). In 3 cases of slow

wrestling over 4 minutes there was no neutrophilic reaction.

3. Swimming from 60 to 220 yards produced an increase in lymphocytes (up to 55%) with a tendency to neutrophily. Longer distances resulted in an increase of neutrophils (up to 78%) with a greater increase of young, non-segmented neutrophils than older, segmented neutrophils.

#### *Conclusions*

1. Increase in the number of the white blood corpuscles is largely due to a redistribution of the blood and release of WBC from the "storage places."

2. Exercise also probably stimulates the release of younger WBC from the bone marrow.

### **180. Keast, D., K. Cameron, and A.R. Morton:**

Exercise and the immune response.

*Sports Medicine* 5:248-267, 1988.

#### *Authors' abstract*

A growing number of reports have become available which implicate infectious disease with reduced performance in athletes. The immune system consists of both nonspecific and specific components geared to control infections. Adaptive immunity functions through both antibody-mediated and cell-mediated compartments to establish and maintain long term immunity to infectious agents. Evidence is accumulating to support the view that physical exercise can lead to modification of the cells of the immune system. However, studies have often not been well designed to control exercise protocols when examining the effects of exercise on the immune system. Large numbers of peripheral blood lymphocytes are mobilized with exercise and *in vitro* tests indicate that temporarily these cells may not be capable of responding normally to mitogens. These reactions appear to be influenced by hormones to some degree and there are reports that the cells of the immune system are extremely active biochemically and may depend on products from muscles to maintain their activity. Specific populations within the circulating leucocyte pool vary significantly with exercise and there is some evidence that the T4/T8 lymphocyte ratio may become significantly reduced. This reduction in ratio may be related to the variable responses to T and B cell mitogens recorded *in vitro* which overall suggests that a temporary immune suppression may exist following certain training or performance schedules. It is argued that this may lead to a temporary susceptibility to infection and could result from overtraining.

**181. Kelso, T.B., W.G. Herbert,  
F.C. Gwazdauskas, F.L. Goss, and  
J.L. Hess:**

Exercise-thermoregulatory stress and increased  
plasma  $\beta$ -endorphin/ $\beta$ -lipotropin in humans.  
*Journal of Applied Physiology* 57:444-449, 1984.

**Authors' abstract**

Six adult male volunteers of similar body composition and physical fitness were tested to determine plasma immunoreactive  $\beta$ -endorphin/ $\beta$ -lipotropin ( $\beta$ -EN/ $\beta$ -LPH) response under three exercise-thermoregulatory stress conditions. The experimental protocol consisted of 120 minutes of stationary upright cycling at 50%  $\dot{V}O_2$  max under neutral (24°C, 50% RH)-euhydration (NE), hot (35°C, 50% RH)-euhydration (HE), and hot-dehydration (HD) environmental conditions.  $\beta$ -EN/ $\beta$ -LPH was calculated by radioimmunoassay at ~30-min, 0-min, and 15-min intervals thereafter. Change in plasma volume (APV) was measured to determine its effect on  $\beta$ -EN/ $\beta$ -LPH concentration. Pre-exercise  $\beta$ -EN/ $\beta$ -LPH levels averaged  $23.7 \pm 2.6$  pg·ml<sup>-1</sup> in all conditions. The greatest  $\beta$ -EN/ $\beta$ -LPH response occurred at 105 min in HD conditions when levels rose to  $43.2 \pm 6.9$  pg·ml<sup>-1</sup>. Exercise in HD and HE conditions resulted in significantly ( $P < 0.05$ ) elevated  $\beta$ -EN/ $\beta$ -LPH above levels observed in NE. APV did not account for more than 10% of  $\beta$ -EN/ $\beta$ -LPH changes at any time interval. The  $\beta$ -EN/ $\beta$ -LPH response pattern closely paralleled rectal temperature changes in all conditions. These data suggest that conditions of increasing exercise thermoregulatory stress are associated with increasing peripheral  $\beta$ -endorphin concentration.

**182. Kendall, A., L. Hoffman-Goetz,  
M. Houston, B. MacNeil, and  
Y. Arumagam:**

Exercise and blood lymphocyte subset responses:  
intensity, duration, and subject fitness effects.  
*Journal of Applied Physiology* 69:251-260, 1990.

**Authors' abstract**

This study examined the effect of exercise intensity and duration on the percent blood lymphocytes in men of low [LF; maximal  $O_2$  uptake ( $\dot{V}O_2$  max) < 50 ml·kg<sup>-1</sup>·min<sup>-1</sup> and sedentary], moderate (MF;  $\dot{V}O_2$  max = 50-60 ml·kg<sup>-1</sup>·min<sup>-1</sup> and recreationally active), and high (HF;  $\dot{V}O_2$  max > 60 ml·kg<sup>-1</sup>·min<sup>-1</sup> and recent training history) fitness. Thirty healthy adult men (aged 20-31 yr) participated in four randomly ordered cycle ergometer rides: *ride 1* (65%  $\dot{V}O_2$  max, 30 min) *ride 2* (30%  $\dot{V}O_2$  max, 60 min), *ride 3* (75%  $\dot{V}O_2$  max, 60 min), and

*ride 4* (65%  $\dot{V}O_2$  max, 120 min). Blood samples were drawn at various times before and after exercise sessions. Lymphocyte subsets were determined by flow cytometry using monoclonal antibodies for total T (CD3+), T-helper (CD4+), and T-suppressor (CD8+) lymphocytes and for a subset of cells expressing a natural killer (NK) cell antigen (Leu7+). Plasma catecholamines were assayed to determine exercise stress. There were sharp reductions ( $P < 0.01$ ) in the percentage of pan-T and T-helper lymphocytes immediately after exercise across all fitness levels; the magnitude of this reduction was greatest after the highest intensity (*ride 3*) or longest duration (*ride 4*) work. In contrast, the absolute number of T and T-helper cells tended to increase after exercise and significantly so in the HF subjects ( $P < 0.005$ ). There was no significant effect of exercise or subject fitness category on the percentage of T-suppressor lymphocytes, although the absolute numbers of this subset increased significantly after exercise in LF subjects. Marked increases ( $P < 0.01$ ) in the percentages of NK cells occurred immediately after exercise at all intensities and durations tested; numerical increases in total NK cells were significant in all fitness groups after the highest intensity work (*ride 3*;  $P < 0.005$ ). Irrespective of whether the changes were expressed as percentage or total numbers, recovery to base line occurred at 30 min after exercise. The results suggest that the exercise effect on blood lymphocyte subset percentages in men is transient and occurs across all fitness levels. Concomitant changes in plasma catecholamine concentrations are only weakly associated with these lymphocyte subset percentage responses to exercise. Furthermore, this study shows that the exercise-induced changes in lymphocyte percentages do not consistently reflect changes in the absolute numbers of cells.

**183. Khoo, H.E., R. Yuen, K.P. Fung:**

Plasma and lymphocyte cyclic nucleotide response to acute exercise in healthy adults.  
*Journal of Sports Medicine and Physical Fitness*  
31:204-207, 1991.

**Authors' abstract**

Plasma and lymphocyte nucleotide levels were assayed in 11 (5 male, 6 female) healthy normal adults before and after bicycle ergometry exercise. Lymphocytosis after exercise was observed. Plasma cAMP level was increased by almost 2 fold after exercise. However, plasma cGMP level was not affected. On the contrary, lymphocytic cAMP level was decreased by one third while cGMP level was halved. There were linear regression relationships between maximum heart rate and % difference in lymphocyte count and lymphocytic cyclic

nucleotide levels pre- and post-exercise. Our findings demonstrate that higher cardiac output leads to increased lymphocytosis but decreased lymphocytic cyclic nucleotide levels.

**184. Kiel, R.J., F.E. Smith, J. Chason,**

**R. Khatib, and M.P. Reyes:**

Coxsackievirus B3 myocarditis in C3H/HeJ mice:

Description of an inbred model and the effect of exercise on virulence.

*European Journal of Epidemiology* 5:348-350, 1989.

**Authors' abstract**

The effect of forced exercise on the development of coxsackie virus B3 myocarditis in inbred C3F/HeJ mice was studied. Four groups of mice (30 per group) were formed: infected-exercised (Group I); infected-unexercised (Group II); uninfected-exercised (Group III); and uninfected-unexercised (Group IV). Infected mice were inoculated intraperitoneally with  $1.0 \times 10^{2.1}$  TCID<sub>50</sub> coxsackievirus B3. Exercised animals were swum daily for 60 minutes on days 1-9. Myocardial viral titers were acutely elevated on day 3 of infection and were augmented significantly by exercise on days 6 and 9. Exercise increased the overall mortality from 0-10% to 20-40%; significantly increased heart:body weight ratios on days 6, 9, and 13; and increased the extent of myocardial fiber necrosis. We have reproduced the acceleration of CB3 myocarditis by exercise in the inbred C3H model.

**185. Klurfeld, D.M., C.B. Welch, E. Einhorn, and D. Kritchevsky:**

Inhibition of colon tumor promotion by caloric restriction or exercise in rats.

*FASEB Journal* 2:A433, 1988.

**Authors' abstract**

Caloric restriction (CR) significantly inhibits colon tumor formation. It is unknown if reduced weight gain of equal magnitude due to either exercise or CR would have equivalent effects of tumorigenesis. This study compared the effects of CR and treadmill exercise (24 m/min  $\times$  60 min  $\times$  5 d/wk) equal caloric expenditure to 25% of oral intake on tumor formation during the promotion phase induced by dimethylhydrazine in male F344 rats. Treatments were: 1) ad libitum (AL)-sedentary (Sed); 2) AL-exercise (Ex); 3) 25% CR-Sed; 4) 25% CR-Ex; and 5) 40% CR-Sed. The restricted diets provided equal nutrient intake (except carbohydrate) in all groups. Groups 1 and 2 consumed equal calories. Body weights of groups 2 through 5 were 18, 25, 37, and 40% less than

Al-Sed. Colon tumor incidence in the 5 groups, respectively, was 75, 36, 35, 29, and 21% ( $p < 0.007$ ). Intestinal transit time as measured by chromic oxide marker was reduced in both exercise groups ( $p < 0.05$ ). Fecal bile acids and stool volume were unaffected by treatment. Analysis of body composition showed the following percentages of lipid: 1) 21.8; 2) 21.6; 3) 13.0; 4) 8.3; and 5) 8.0. Group 2 had adiposity similar to group 1 but half the tumor incidence; group 3 had tumor incidence equal to group 2 but significantly less body fat. These results show that exercise can reduce colonic carcinogenesis significantly and that this effect is related to body weight and probably to lean body mass rather than adipose tissue mass.

**186. Kobasa, S.C.O., S.R. Maddi, M.C. Puccetti, and M.A. Zola:**

Effectiveness of hardiness, exercise and social support as resources against illness.

*Journal of Psychosomatic Research* 29:525-533, 1985.

**Authors' abstract**

The effects of the resistance resources of personality hardiness, exercise, and social support, taken singly and in combination, on concurrent and prospective levels, and probability of illness were studied. In 1980, 85 male business executives identified as high in stressful events were tested for the three resistance resources. Predicting their illness scores in 1980 formed the concurrent aspect of the study. For the prospective aspect, illness scores in 1981 were available on 70 of the subjects. With regard to resistance resources, when there are none, one, two or three, the level and probability of both concurrent and prospective illness drop in a regular and marked fashion. These results highlight the importance of multiple resistance resources. Estimates of relative effectiveness indicate that hardiness is the most important of the resistance resources studied.

**187. Kohl, H.W., R.E. LaPorte, and**

**S.N. Blair:**

Physical activity and cancer. An epidemiological perspective.

*Sports Medicine* 5:222-237, 1988.

**Authors' summary**

Relatively little is known about the role that increased physical activity may have in protecting humans from malignancy. Herein, studies are reviewed on the basis of the type of physical activity exposure studied: occupational or leisuretime. Results suggest that if any



consistencies emerge, there may be a protective effect of increased physical activity exposure upon cancer of the colon, and no effect on cancer of the rectum, in men. Increased physical activity in women during college years may protect against certain reproductive system cancers. Methodological deficiencies in assessment of physical activity (total exposure over lifetime) and in lack of control for other potential explanations block further, more solid conclusions. The fact that an association has been demonstrated in spite of these drawbacks, however, indicates the importance of further study. Suggested directions for future work are presented.

**188. Kokot, K., R.M. Schaefer, M. Teschner, U. Gilge, R. Plass, and A. Heidland:**

Activation of leukocytes during prolonged physical exercise.

*Advances in Experimental Medicine and Biology*  
240:57-63, 1988.

**Authors' abstract**

Previous studies have demonstrated an increment of circulating leukocytes and enhanced secretion of interleukin-1 by monocytes and macrophages during physical exercise. In the present study the effect of physical exertion on the activity of polymorphonuclear (PMN) leukocytes was investigated. Following both short-term (running 2,000 meters) and long-term (running 10,000 meters) exertion, phorbol-stimulated chemiluminescence, as an indicator of leukocytic oxygen radical formation and release of leukocytic elastase, as a parameter of degranulation, were determined immediately after running. The number of circulating leukocytes increased both after short-term (+21%) and long-term (+61%) exercise. There was a minor release of PMN elastase following short-term activity causing plasma levels of this compound to rise from  $100 \pm 4.0$  ng/ml to  $116 \pm 12.3$  ng/ml. Long-term exercise, on the other hand, induced a significant increase of elastase plasma level from  $107 \pm 9.1$  ng/ml to  $300 \pm 23.4$  ng/ml, suggesting a remarkable release of this proteinase from neutrophils. Based on these findings we conclude that, during physical exercise, degranulation of PMN leukocytes occurs. Moreover, the fact that phorbol-stimulated chemiluminescence is decreased after running demonstrates an impaired capability of white cells to generate oxygen radicals.

**189. Kolyada, T.I., L.N. Abzaeva,**

**Yu.A. Baboshko, and A.F. Ershov:**

Effects of exercise, hypoxia, and hyperthermia on the cellular anti-infection resistance factors of the body.  
*Zhurnal Mikrobiologii, Epidemiologii i Immunologii*  
2:76-79, 1988.

**Authors' summary**

Examinations of 146 healthy males aged 20-25 years have shown that moderate exercise stimulates the function of peripheral macrophages. The same effect is produced by exercise in combination with a single exposure to hypoxia. On the contrary, combined exposure to exercise, hypoxia and hyperthermia leads to the development of a tendency towards the suppression of macrophagal phagocytosis. The functional loading of the body induces deep transformation of the structure of the correlative characteristics of phagocytosis and hemogram.

**190. Konstantinova, I.V.:**

The immune system under extreme conditions: Space immunology.

In: *Problemy Kosmicheskoy Biologii*, no. 59.  
Moscow: Nauka Press, 1988. p. 125-149.

**Author's abstract**

At the beginning of the 1960s, it was concluded on the basis of bedrest studies that hypokinesia decreases general resistance. The author and associates studied the dynamics of changes in immune response in ground-based studies modeling the effects of weightlessness using hypokinesia with head down tilt. Immune status of healthy individuals was studied before, during, and after exposure to 182, 120, 35, and 8 days of treatment. The first such study involved a 182-day period of hypokinesia and 18 healthy males divided into three groups. The first group was treated with a set of prophylactic measures similar to those developed for space flight, including physical exercise (twice a day for 60 minutes with energy cost of 350-400 cal/hr). The second group followed an abbreviated exercise program (20 minutes per day). Both groups were treated with lower body negative pressure and salt water supplements. No prophylactic measures were used for the third group. Two 120-day studies utilized 21 individuals, with a head-down tilt angle of  $4.5^\circ$ . Some of these subjects were treated with prophylactic measures. Six healthy women participated in the 35-day study. Of these, three engaged in a special set of physical exercises. Eight women participated in another 8-day study. In the 182-day study, levels of E-RFC and EAC-RFC remained unchanged in all three groups. Eight individuals displayed a short-lived decrease in concentration of T-lymphocytes on day 40. Concentration

of B-lymphocytes decreased moderately in 11 of 18 individuals during the first 1-1.5 months of treatment; this change was not associated with group membership. The 120- and 35-day studies had similar results. E-RFC level was depressed in some subjects on day 70 but then normalized. Other parameters were unchanged. PHA reactivity, which under normal conditions is quite labile, decreased in 15/18 subjects of the 182-day study, but only to a moderate extent. In this study certain subjects were affected by various minor ailments, boils, colds, periodontitis, etc. These ailments tended to coincide with the period of diminished PHA reactivity. Moderate decreased response to PHA was also found in the 120-day studies. Short-term (8-day) hypokinesia was not associated with decreased PHA reactivity. Activity of natural killer cells measured using the Index of Cytotoxicity (IC) decreased during certain periods of hypokinesia. Study of individual patterns created the impression that there were two different response types. In some subjects decrease in IC occurred after 1-1.5 months of treatment, and continued to decrease until treatment stopped at the end of 4 months, normalizing after treatment, but cytotoxicity of natural killers decreased immediately after termination. In another study, cytotoxicity of natural killers decreased in five of eight females subjects on day 7 of an 8-day period of hypokinesia. Some women also showed decreased IC after treatment terminated. Activity of T-helpers, estimated on the basis of the xenographic graft vs host reaction, underwent few significant changes. Nonspecific suppressor activity of T-lymphocytes was elevated during some periods of hypokinesia in some subjects, even during the shortest hypokinesia study. Previous studies indicated that allergic hypersensitivity might develop during prolonged periods of hypokinesia. In the experiment imposing 182 days of hypokinesia with head-down tilt, the method of specific blastogenesis with a number of bacterial allergens, as well as skin tests with the same allergens, was used to determine allergic responses. Allergens used included staphylococcus, streptococcus, proteus, and intestinal bacilli. Tests of *in vitro* response of lymphocytes were performed six times for each subject. During hypokinesia, 7 of 18 subjects displayed signs of developing sensitization to various bacterial allergens. The period preceding the appearance of positive reactions varied from 1.5 to 3 months. In four subjects, continued hypokinesia was accompanied by allergic response to additional allergens. There was no difference between subjects showing allergic sensitivity and those without such sensitivity with respect to number or duration of most bacterial or viral ailments developed during hypokinesia. Furuncles (boils) lasted significantly longer in subjects showing allergic sensitivity. When individual subjects were considered, a clear relationship was noted between the course of an ailment like boils and

disruption of immune response. Tests using inhibition of leukocyte migration reaction as an indicator confirmed the occurrence of new allergic responses during the latter stages of a 120-day hypokinesia period in 8/21 subjects.

**191. Kotani, T., Y. Aratake, R. Ishiguro, I. Yamamoto, Y. Uemura, K. Tamura, and S. Ohtaki:**

Influence of physical exercise on large granular lymphocytes, Leu-7 bearing mononuclear cells and natural killer activity in peripheral blood—NK-cell and NK-activity after physical exercise.

*Acta Haematologica Japonica* 50:1210-1216, 1987.

**Authors' abstract**

The number of large granular lymphocytes, Leu-7 positive mononuclear cells and the activity of natural killer cells were studied sequentially after treadmill exercise. The number of large granular lymphocytes and Leu-7 positive mononuclear cells increased immediately after exercise, and returned to the initial level by 30 min after exercise. Similar findings were observed, but natural killer-activity did not return to the initial level 30 min after the second trial. These findings suggest that functional activity of natural killer cells differs with time after exercise despite having the same number of natural killer cells.

**192. Krawietz, W., E.M. Klein, Ch. Unterberg, and M. Ackenheil:**

Physical activity decreases the number of  $\beta$ -adrenergic receptors on human lymphocytes.

*Klinische Wochenschrift* 63:73-78, 1985.

**Authors' abstract**

On intact human lymphocytes a specific binding site (BS) for  $^{125}\text{I}$ -Cyanopindolol ( $^{125}\text{I}$ -CYP), a derivative of the  $\beta$ -blocking drug pindolol, was characterized. Inhibition of binding for catecholamines in the following order of potency: l-isoprenaline > l-adrenaline > l-noradrenaline proves the BS as a  $\beta_2$ -receptor subtype. In 77 healthy persons (36 females, 41 males) the number of BS amounted to  $2,639 \pm 125$  BS/cell without any significant correlation to age (17-86 years) or sex. The dissociation constant (KD) indicating the affinity of iodo-cyanopindolol to the BS on intact lymphocytes was  $\text{KD} = 1.9 \pm 1.1 \times 10^{-10}\text{M}$ . A change of the number of  $\beta$ -receptors on intact human lymphocytes has been measured previously in asthmatics and in the myocardium of patients with congestive heart failure. We investigated a possible change in the  $\beta$ -receptors on lymphocytes by physical and mental activity ("stress") in physicians going

about their daily routine work. Persons left alone in a hospital room reading or sleeping were defined as "inactive controls". The number of BS on intact lymphocytes was significantly higher in active persons at 8 a.m. ( $2,230 \pm 482$  BS) compared to active persons at 1,743  $\pm$  285 BS;  $P < 0.05$ ) and at 1 p.m. ( $2,394 \pm 253$  BS vs 1,733  $\pm$  556;  $P < 0.05$ ) but not different at 6 p.m. ( $1,634 \pm 578$  BS vs 1,768  $\pm$  588 BS;  $P < 0.01$ ). The K<sub>D</sub> remained unchanged under all conditions. The serum noradrenaline and adrenaline levels were also measured during the day. The serum adrenaline levels were higher in the active group than in the inactive group at 8 a.m. ( $46 \pm 11$  pg/ml vs  $22 \pm 8$  pg/ml;  $P < 0.01$ ) and at 1 p.m. ( $36 \pm 13$  pg/ml vs  $13 \pm 5$  pg/ml;  $P < 0.01$ ) but not at 6 p.m. ( $37 \pm 28$  pg/ml vs  $13 \pm 6$  pg/ml;  $P < 0.1$ ). Our data clearly show higher serum adrenaline levels but fewer BS on intact human lymphocytes in active persons than in inactive persons at 8 a.m. and 1 p.m. The high catecholamine serum levels may cause a down-regulation of the number of  $\beta$ -receptors in the active persons.

### 193. Krikler, D.M. and B. Zilberg:

Activity and hepatitis.  
*Lancet* 2:1046-1047, 1966.

#### Authors' abstract

Five patients with fulminant hepatitis had all undertaken vigorous physical activity during the early stages of the illness. Exercise may have made mild attacks severe, and strenuous exertion should be avoided when early hepatitis is suspected.

### 194. Kritchevsky, D.:

Influence of caloric restriction and exercise on tumorigenesis in rats.  
*Proceedings of the Society for Experimental Biology and Medicine* 193:35-38, 1990.

#### Author's abstract

Underfeeding or caloric restriction have been shown to inhibit the growth of spontaneous, transplanted, or chemically induced tumors in rats and mice. At 40% caloric restriction, growth of 7,12-dimethylbenz(a)anthracene-induced mammary and 1,2-dimethylhydrazine-induced colonic tumors is inhibited significantly even when the restricted diet contains twice as much fat as the control diet. Some inhibitory effects become evident even at 10% caloric restriction. In studies involving high fat diets, we find that rats receiving 20% fat *ad libitum* exhibit significantly higher 7,12-dimethylbenz(a)anthracene-induced mammary tumor incidence, multiplicity, and weight than rats

ingesting the same amount of fat daily, but in a diet containing 25% fewer calories. In a study of intermittent *ad libitum* and restrictive feedings, chemically induced tumorigenicity varies inversely with feed efficiency. Exercise has also been shown to inhibit tumor growth. Sedentary rats fed *ad libitum* have a 108% higher incidence of 1,2-dimethylhydrazine-induced colon tumors than rats fed *ad libitum* but subjected to vigorous treadmill exercise. Caloric flux (either reduced intake or increased outflow) appears to reduce tumorigenicity in rodents.

### 195. Landmann, R.M.A., F.B. Müller,

Ch. Perini, M. Wesp, P. Erne, and  
F.R. Bühler:

Changes of immunoregulatory cells induced by psychological and physical stress: relationship to plasma catecholamines.  
*Clinical and Experimental Immunology* 58:127-135, 1984.

#### Authors' abstract

Lymphocyte subpopulations were measured before and after physical and psychological stress in 15 healthy subjects, and correlated with plasma catecholamine and cortisol levels. During psychological stress monocytes ( $P < 0.05$ ), NK ( $P < 0.01$ ), B cells ( $P < 0.05$ ) and heart rate ( $P < 0.001$ ) increased, while catecholamines remained unchanged. With physical stress, granulocytes, monocytes, and all lymphocyte subsets increased significantly, although B cells rose more than T cells and T (suppressor) cells more than T (helper) cells. Thus, the ratio of T/B cells and of Th/Ts cells decreased ( $P < 0.001$  and  $P < 0.01$ ). Adrenaline and noradrenaline concentrations increased ( $P < 0.001$ ), while cortisol remained unchanged. There was a negative relationship between adrenaline and the Th/Ts cell ratio before and after stress ( $P < 0.05$ ). Lymphocyte subpopulations from a different group of 4 healthy subjects were analyzed before and after isoproterenol infusion. There was a small increase in Ts and B cells only ( $P < 0.1$ ) and a decrease of the T/B cell ratio ( $P < 0.05$ ). The predominant enrichment of circulating B, Ts and NK cells during short lasting adrenergic activation, as well as the relationship of the T cell changes to plasma adrenaline, suggests an immunoregulatory effect of the sympathetic nervous system in stress.

**196. Landmann, R., M. Portenier,**

**M. Staehelin, M. Wesp, and R. Box:**

Changes in  $\beta$ -adrenoceptors and leukocyte subpopulations after physical exercise in normal subjects.

*Naunyn-Schmiedeberg's Archives of Pharmacology* 337:261-266, 1988.

**Authors' abstract**

Seven healthy volunteers were subjected to standardized bicycle ergometry. Before and at the end of exercise, leukocyte and lymphocyte subset distribution was assessed by immunofluorescence labelling with monoclonal antibodies and the cytofluorograf. Competition binding studies were performed in mononuclear leukocytes with a fixed amount of the radioligand  $^{125}\text{I}$ -(-)-cyanopindolol ( $^{125}\text{I}$ -CYP) and increasing concentrations of the hydrophobic ligand (-)-4-(3-tertiary-butylamino-2-hydroxypropoxy)-benzimidazol-2-one hydrochloride (CGP-12177). Total numbers of  $\beta$ -adrenoceptors per cell and the receptor-ligand affinities were then derived by computer analysis. In separate experiments with blood obtained from resting subjects,  $\beta$ -adrenoceptor numbers of lymphocyte subsets, which had been sorted by the fluorescence activated cell sorter, were determined by a saturation binding of  $^{125}\text{I}$ -CYP. During exercise there was a two-fold increase in total leukocyte numbers. The ratio between monocytes (4%) and lymphocytes (55%) remained constant, but the composition of lymphocyte subsets had changed. A two-fold increase was observed for the lymphocyte population carrying the Leu-7 antigen, whereas the number of B cells and CD4-positive T cells increased only slightly. The lymphocyte phenotype changes appeared after 3 min, reached a maximum at the end of ergometry and had disappeared 30 min after exercise. Exercise led to a doubling of the number of leukocytes from  $240 \pm 46$  to  $535 \pm 190$  sites per cell (SD,  $n = 6$ ).  $\beta$ -adrenoceptor numbers were higher on sorted Leu-7 positive cells ( $K_D$   $14 \pm 6$  pmol/l,  $B_{\text{max}}$   $1174 \pm 233$  sites/cell) and on CD8 positive cells ( $K_D$   $145 \pm 79$  pmol/l,  $B_{\text{max}}$   $1577 \pm 670$  sites/cell) than on monocytes ( $K_D$   $39 \pm 31$  pmol/l,  $647 \pm 91$  sites/cell). Very low specific  $^{125}\text{I}$ -CYP binding was found on Leu-7 and CD8 negative cells (less than 0.2 pmol/l). Before exercise the displacement curves with CGP-12177 fitted best a single site model, whereas after exercise 12% of the receptors were in a low affinity state for CGP-12177, indicating internalized receptors. The extent of internalization, however, was rather small (12%) compared to that found in experiments *in vitro* (66% of receptors in a low affinity state). The present study shows for the first time that exercise induces an increase in

$\beta$ -adrenoceptor numbers per cell on mononuclear leukocytes and, at the same time, an alteration in the distribution of lymphocyte subsets in blood with a predominant enrichment of a population carrying many high affinity  $\beta$ -adrenoceptors.

**197. LaPerriere, A.R., M.H. Antoni,**

**N. Schneiderman, G.I. Ironson,**

**N. Klimas, P. Caralis, and M.A. Fletcher:**

Exercise intervention attenuates emotional distress and natural killer cell decrements following notification of positive serologic status for HIV-1. *Biofeedback and Self-Regulation* 15:229-242, 1990.

**Authors' abstract**

The impact of aerobic exercise training as a buffer of the affective distress and immune decrements which accompany the notification of HIV-1 antibody status in an AIDS risk group was studied. Fifty asymptomatic gay males with a pretraining fitness level of average or below (determined by predicted  $\text{VO}_2$  max) were randomly assigned to either an aerobic exercise training program or a no-contact control condition. After 5 weeks of training, at a point 72 hours before serostatus notification, psychometric, fitness and immunologic data were collected on all subjects. Psychometric and immunologic measures were again collected one week postnotification. Seropositive controls showed significant increases in anxiety and depression, as well as decrements in natural killer cell number following notification, whereas seropositive exercisers showed no similar changes and, in fact, resembled both seronegative groups. These findings suggest that concurrent changes in some affective and immunologic measures in response to an acute stressor might be attenuated by an experimentally manipulated aerobic exercise training intervention.

**198. LaPerriere, A., M.A. Fletcher,**

**M.H. Antoni, N.G. Klimas, G. Ironson,**

**and N. Schneiderman:**

Aerobic exercise training in an AIDS risk group. *International Journal of Sports Medicine* 12:S53-S57, 1991.

**Authors' abstract**

Increases in physical fitness are often associated with improvements in certain chronic diseases, such as hypertension and coronary heart disease. Recent evidence has shown that exercise also influences the neuro-endocrine and immune systems, resulting in a potential to benefit those with chronic immunodeficiency diseases. Therefore, exercise may prove to have a profound impact

on the management of the acquired immunodeficiency syndrome (AIDS). Our current work includes the investigation of the immunologic and stress-attenuating effects of an aerobic exercise training program for individuals at risk for AIDS. Upon completion of training, the subjects showed a significant increase in helper/inducer (CD4) cells and the inducer subset (CD45RA = CD4+) which activate suppressor/cytotoxic (CD8) cells. These increases, which average about 50 cells per cubic millimeter, are comparable to those observed in some studies of the AIDS drug azidothymidine (AZT), but without the accompanying side effects. Also, individuals undergoing aerobic training reported no increases in anxiety and depression in response to notification of a positive HIV serologic status. These findings taken together indicate that an aerobic exercise training program may enhance certain critical components of cellular immunity as well as acting as a buffer for the detrimental mood changes that typically accompany stress, thus providing a timely, promising behavioral approach to helping HIV-1-infected individuals.

**199. LaPerriere, A., P. O'Hearn, G. Ironson,**

**P. Caralis, A. Perry, N. Klimas,**

**N. Schneiderman, and M.A. Fletcher:**

Aerobic exercise training and immune function in healthy HIV antibody negative and positive gay males.

*Proceedings of the 9th Society of Behavioral Medicine*, Boston, MA, 1988.

#### **Authors' abstract**

Healthy gay males (n = 39) never tested and therefore not knowing their human immunodeficiency virus (HIV) status, were randomly assigned to control (n = 17) or exercise (n = 22) groups for a 10 week study. Both groups received a fitness evaluation and immune function analysis at weeks 0, 5 and 10. HIV antibody status was determined at week 5, and subjects received news of their status 72 hours later. After 5 weeks, HIV antibody negative and positive subjects showed a significant improvement in aerobic fitness (max  $\dot{V}O_2$ ) which they maintained during the next 5 weeks, whereas all control subjects displayed no significant change in max  $\dot{V}O_2$  at any time during the study. Aerobic exercise training resulted in a significant increase in CD4 (T4 helper/inducer) cells for both HIV antibody negative [940 to 1110 net counts per min (cpm),  $t(1,9) = 2.6$ ,  $P < 0.05$ ] and positive [915 to 1010 cpm,  $t(1,6) = 2.2$ ,  $P < 0.05$ ] subjects. Additionally, only HIV antibody negative subjects showed a significant increase in the subset of CD4 cells which activates CD8 (T8-cytotoxic/

suppression) cells (2H4 +T4+) [4.3 to 5.8%,  $t(1,9) = 3.4$ ,  $P < 0.05$ ] and mature B cells [7.1 to 19.7%,  $t(1,9) = 3.6$ ,  $P < 0.05$ ] indicating that their immune system may be more responsive to aerobic exercise training. These data offer preliminary evidence that HIV antibody negative subjects clearly show beneficial effects of an aerobic exercise training program on immune function, whereas HIV antibody positive subjects may derive some immune enhancement, but to a lesser extent. This may be due in part to the immune system of HIV antibody positive subjects being compromised even before overt symptoms occur. This is supported by the finding that at initial screening, prior to aerobic training, HIV antibody positive subjects were significantly lower than HIV antibody negative subjects in terms of natural killer cells as determined with monoclonal antibody NKH-1 [6.9 vs. 10.9%,  $E(1,36) = 4.2$ ,  $P < 0.05$ ], CD4 cells [844 vs. 1175 (cpm),  $E(1,34) = 5.6$ ,  $P < 0.05$ ], T4/T8 ratio [76 vs. 1.6,  $E(1,35) = 24.6$ ,  $P < 0.05$ ], lymphocyte response to Pokeweed mitogen [1649 vs. 3746 cpm,  $E(1,36) = 6.9$ ,  $P < 0.05$ ] lymphocyte response to Phytohemagglutinin [35514 vs. 61930 cpm,  $E(1,37) = 4.6$ ,  $P < 0.05$ ], and significantly higher in terms of CD8 cells [1182 vs. 782 cpm,  $E(1,34) = 0.01$ ,  $P < 0.05$ ].

**200. LaPerriere, A., N. Schneiderman,**

**M.H. Antoni, and M.A. Fletcher:**

Aerobic exercise training and

psychoneuroimmunology in AIDS research.

In: *Psychological Perspectives on AIDS*, edited by

A. Baum, and L. Temoshok. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc., 1990. p. 259-286.

#### **Authors' summary**

Our data offer evidence that HIV-1 negative subjects clearly show beneficial immunologic effects of aerobic exercise training by an increase in  $\beta$ -cells, CD4+ cells and the 2H4+T4+ subset. HIV-1 positive subjects also show some immunologic enhancement, although to a lesser extent, by an increase in CD4+ cells only. The attenuated immunologic augmentation seen in HIV-1 positive subjects may indicate that their already compromised immune system is less responsive to exercise training. However, the increase in CD4+ cells shown by HIV-1 positive subjects is comparable to the magnitude of increase seen in studies of AZT administration (Yarchoan et al., 1988a, 1988b), but without the accompanying side effects. Furthermore, the buffering effect of aerobic exercise training displayed in HIV-1 positive subjects appears to indicate that aerobic exercise training may prove to be an appropriate stress-management technique yielding immunologic (i.e., attenuated NK cell decrease to a stressor) and psychosocial benefits in this population.

It would thus appear that HIV-1 can be viewed as a chronic disease for which early immunomodulatory behavioral interventions, such as aerobic exercise training, may have important physical and psychological impact, including the slowing of disease progression, reduction of opportunistic infections, and improved quality of life.

## 201. Larrabee, R.C.:

Leukocytosis after violent exercise.  
*Journal of Medical Research* 7:76-82, 1902.

### Synopsis

**Purpose** To study the effect of prolonged, violent exercise on leukocytosis.

### Methods

1. Four runners of the 1901 Boston Athletic Association's Marathon race, of about 25 miles, were studied.
2. Blood samples were taken before the race and within 5 minutes after the race.

### Results

1. Leukocytosis was found in every subject varying from 14,400 to 22,200.

2. The differential count showed that the increase was mainly in the polymorphonuclear neutrophils. Eosinophils were both relatively and absolutely diminished.

3. In 3 of the 4 subjects, a few myelocytes (mononuclear cells with neutrophilic granules) were found.

### Conclusions

1. Violent, prolonged exhausting work produces a leukocytosis.
2. The leukocytosis is caused by an increase in polymorphonuclear cells, but other cells may also be considerably increased in numbers.
3. More than one factor acts to produce the leukocytosis; probably a temporary mechanical cause, and a toxic cause, slower to develop, but lasting the duration of the exercise.

## 202. Leeds, E.M., J.M. Pivarnik, and

J.E. Wilkerson:

Exercise leukocytosis and WBC differential during endurance exercise.

*Federation Proceedings* 42:335, 1983.

### Authors' abstract

Six healthy adult males each ran on a motor-driven treadmill on 3 separate occasions: for 1 hour at 40% and 60% of their measured aerobic capacities ( $\dot{V}O_2$  max = 64.5 ml/kg/min), and to exhaustion at 80%  $\dot{V}O_2$  max. Blood samples were drawn by venepuncture before and after each exercise bout and analyzed for hematocrit (Hct), whole blood hemoglobin concentration (Hb), leukocyte count (LC) and white cell differential (WCD). Neither LC nor total number of circulating leukocytes was related to relative exercise intensity (%  $\dot{V}O_2$  max). There was little change in the WCD following the 40%  $\dot{V}O_2$  max bout with a 15% leukocytosis. At 60%  $\dot{V}O_2$  max there was a 21% leukocytosis with a large neutrophilia and a lymphocytosis. At each work level there was relatively the same magnitude of decrease in total eosinophils with no change in the total number of circulating monocytes or basophils. There was a linear increase in the number of circulating neutrophils with increasing relative exercise intensity, with a lymphocytosis noted only at the 80%  $\dot{V}O_2$  max level. These data are not consistent with the postulation of the development of 3 phases of exercise leukocytosis. Rather, there appear to be two mechanisms operating: a linear one related to exercise intensity (neutrophilia) and another with an apparent threshold of response at the level of the anaerobic threshold (leukocytosis).

## 203. Levinson, S.O., A. Milzer, and P. Lewin:

Effect of fatigue, chilling, and mechanical trauma on resistance to experimental poliomyelitis.

*American Journal of Hygiene* 42:204-213, 1945.

### Authors' abstract

1. Monkeys subjected to exhausting exercise during the incubation period of experimental poliomyelitis developed a higher incidence and more severe paralysis than controls.
2. Monkeys subjected to chilling during the incubation period of experimental poliomyelitis also developed a higher incidence and more severe paralysis than controls.
3. Monkeys subjected to trauma of one or more limbs during the incubation period of experimental poliomyelitis showed no correlation with location of paralysis, and the severity or extent of paralysis did not differ from the controls.

4. The incidence and severity of paralysis was significantly greater in monkeys with poliomyelitis during the summer months.

**204. Lewicki, R., H. Tchorzewski, A. Denys, M. Kowalska, and A. Golinska:**

Effect of physical exercise on some parameters of immunity in conditioned sportsmen.  
*International Journal of Sports Medicine* 8:309-314, 1987.

**Authors' abstract**

The studies were performed on 20 conditioned cyclists and 19 untrained men. At rest absolute and percent number of neutrophils, eosinophils, and monocytes, neutrophil bactericidal activity, and blood plasma B-glucuronidase, acid phosphatase, and lactic dehydrogenase (LDH) activities were similar in sportsmen and untrained men, while neutrophil adherence was lowered in sportsmen. Maximal physical exercise induced significant rises in absolute numbers of neutrophils and monocytes in both groups. In sportsmen, adherence of neutrophils and monocytes and neutrophil bactericidal activity significantly decreased under the influence of exercise, while neutrophil phagocytic activity did not change. On the other hand, in untrained men, maximal physical exercise did not induce significant changes in neutrophil and monocyte adherence and bactericidal activity of neutrophils, but their phagocytic activity increased. Blood plasma B-glucuronidase, acid phosphatase, and LDH activities increased during exercise in both groups. The changes observed tended to normalize during 2-h recovery. The results obtained suggest that intensive physical exercise tends to suppress nonspecific immunity, which may render sportsmen more susceptible to infections.

**205. Lewicki, R., H. Tchorzewski, E. Majewska, Z. Nowak, and Z. Baj:**

Effect of maximal physical exercise on T-lymphocyte cell populations and on interleukin 1 (IL 1) and interleukin 2 (IL 2) production in vitro.  
*International Journal of Sports Medicine* 9:114-117, 1988.

**Authors' abstract**

Maximal physical exercise was performed on a Monark bicycle ergometer according to individual schemes. The investigations were carried out on 11 highly trained cyclists, aged  $20 \pm 1$  years. Heart rate (HR) amounting to about 200 bts/min and oxygen consumption stabilization were considered as criteria for maximal physical exercise.

Lymphocyte phenotypes were determined using monoclonal antibodies. A significant increase in T<sub>s</sub> (suppressor, cytotoxic) and a moderate increase in T<sub>h</sub> (helper, inducer) and NK (natural killer) cell numbers were noted 3 min after maximal physical exercise. At the same time, a significant diminution of the T<sub>h</sub>/T<sub>s</sub> ratio was observed. A significant increase of interleukin 1 production and a diminished interleukin 2 production as well as spontaneous interleukin 2 receptor expression (Tac antigen) were observed at the same time. After a 2-h recovery, there was a normalization of most of the parameters investigated. The results suggest that maximal physical exercise in highly trained bicycle racers generates transient changes in immune cell function.

**206. Liesen, H., B. Dufaux, and W. Hollmann:**

Modifications of serum glycoproteins the days following a prolonged physical exercise and the influence of physical training.  
*European Journal of Applied Physiology* 37:243-254, 1977.

**Authors' abstract**

Eight male subjects (mean age  $24.1 \pm 2.6$  years) performed at intervals of 2 weeks successively a 3-h and two 2-h runs of different running speed. The days following the running there were moderate elevations of C-reactive protein, haptoglobin, alpha-1-acid glycoprotein, ceruloplasmin, transferrin, alpha-1-antitrypsin and plasminogen. There were small or no changes of albumin, alpha-2-macroglobulin and hemoexin. The elevations of the "acute phase reactants" were examined in three male subjects following a 2-h run before and after an endurance training period of 9 weeks. This demonstrated a decreased acute phase response after training as illustrated by the changes of C-reactive protein, haptoglobin and alpha-1-acid glycoprotein in spite of higher posttraining running speeds. Well-trained athletes have elevated levels of the serum protease inhibitors alpha-1-antitrypsin, alpha-2-macroglobulin and C1-inhibitor. These antiproteolytic glycoproteins might limit exercise-induced inflammatory reactions.

- 207. Liesen, H., K. Kleiter, S. Mücke, U. Order, W. Widenmayer, and H. Riedel:**

Leukozyten und Lymphozytensubpopulationen bei den Spielern der Feldhockeynationalmannschaft während der Olympiavorbereitung 1988.

*Deutsche Zeitschrift für Sportmedizin* 40:1-8, 1989.

**Authors' abstract**

During the general fitness training and the hockey-specific training for the German men's field hockey team in preparation for the Olympic Games in 1988, we examined the behaviour of the leucocytes and lymphocyte subpopulations (CD3+, DR+, CD3+DR+, CD4+, CD8+, Leu-7+, CD8+Leu-7+) of 11 team members by using flow cytometry. With seven of them, the results could be compared with the findings at the end of a regeneration training phase. Four weeks of general fitness training with twelve training sessions per week led, through the combination of overstrained and possibly excessive physical work loads, to a suppression of the leucocytes and lymphocyte subpopulations (apart from NK cells). During the subsequent hockey training in the preparatory phase there was a further reduction in the number of cells combined with symptoms pointing to the onset of infections of the respiratory tract. Treatment with a phyto-based immunomodulant while continuing training and competitions resulted in an increase in all cell fractions and disappearance of the symptoms.

- 208. Liesen, H., H. Riedel, U. Order, S. Mücke, and W. Widenmayer:**

Zelluläre Immunität bei Hochleistungssportlern.  
*Deutsche Zeitschrift für Sportmedizin* 40:9-14, 1989.

**Authors' abstract**

Counting of leukocytes and lymphocyte subpopulations (CD3+, DR+, CD3+DR+, CD4+, CD8+, Leu-7+, CD8+Leu-7+) was determined by flow cytometry at rest in 125 top performance athletes from long-distance running and the Nordic combination (endurance group; n = 50), professional soccer players and members of the national hockey team (group players; n = 66), and fencers (n = 9). The athletes were undergoing regenerative or graduated intensity-controlled aerobic basic training. Compared with the normal values of healthy untrained young men, the sportsmen had significantly lower counts of total lymphocytes, total T, T-helper and NK cells, as well as a lower T4/T8 ratio. In some cases, there were appreciable differences between the various sports, individual disciplines, and teams. The results of aerobic performance diagnostics and training control indicate a

connection between aerobic capacity and absolute cell count. The lower cell counts can be explained by training-induced adaption and do not appear to be the result of temporary stress-related immuno-suppression.

- 209. Linde, F.:**

Running and upper respiratory tract infections.  
*Scandinavian Journal of Sports Science* 9:21-23, 1987.

**Author's abstract**

Upper respiratory tract infections and overexertion injuries were registered during a one-year period in a group of elite orienteers (n = 44). A non-athletic group matched for sex, age, and occupational distribution acted as a control group with regard to disease frequency. The orienteers had 2.5 upper respiratory infections per year on average against 1.7 in the control group (P < 0.05). The length of the disease periods was on average 7.9 days and 6.4 days, respectively (n.s.). An increased number of overexertion injuries could not be demonstrated in periods with or just after upper respiratory tract infections.

- 210. Liu, Y.G. and S.Y. Wang:**

The enhancing effect of exercise on the production of antibody to *Salmonella typhi* in mice.  
*Immunology Letters* 14:117-120, 1986/1987.

**Authors' abstract**

The effect of long-term regular and moderate exercise on antibody production has been studied in mice. Healthy mice were trained to run for 10 min twice a day, and antibody levels following immunization were compared with those of healthy sedentary control mice. The antibody levels of the running mice were significantly higher than those of the sedentary animals at all times tested, from 1 to 13 wk post immunization. Overall, the antibody titres of the runners were 2.76 times that of the controls. The significance of these findings is discussed.

- 211. Lötzerich, H., H.-G. Fehr, and**

**H.-J. Appell:**

Potentiation of cytostatic but not cytolytic activity of murine macrophages after running stress.  
*International Journal of Sports Medicine* 11:61-65, 1990.

**Authors' abstract**

The influence of physical exercise on the tumortoxicity of peritoneal murine macrophages (PMM) was investigated.



The tumortoxic activity was discriminated into cytostatic and cytolytic effects. Cytostatic activity of PMM on tumor cells in vitro was studied using the proliferation assay of S-180 sarcoma cells. Cytolytic activity was monitored using the method of the slow form of antibody-dependent cellular cytotoxicity (ADCC) on SW 707 tumor cells. After a single exhaustive running session an increased cytostatic activity of PMM was observed as compared to PMM of sedentary animals. In PMM mediated ADCC no difference was detected between trained and untrained animals. It is concluded that physical exercise is a complex stimulus for macrophages that, at least in part, triggers their cytotoxic activity against tumor cells.

## 212. Macha, M., M. Schlafer, and

**M.J. Kluger:**

Human neutrophil hydrogen peroxide generation following physical exercise.

*Journal of Sports Medicine and Physical Fitness* 30:412-419, 1990.

### Authors' abstract

The effects of prolonged, submaximal exercise by seven healthy, untrained individuals on the generation of hydrogen peroxide by neutrophils was studied. Hydrogen peroxide generation by neutrophils isolated from pre-exercise (control) and post-exercise blood samples was measured 10, 15 and 20 minutes following stimulation with phorbol myristate acetate (PMA). Exercise was associated with a significant elevation in the number of circulating neutrophils and a diminished capacity for neutrophil hydrogen peroxide generation following PMA stimulation. Addition of post-exercise plasma to neutrophils isolated from pre-exercise blood caused a small reduction in hydrogen peroxide generation, suggesting the presence of an inhibitory factor(s) in the plasma during physical exercise. These results support the concept that exercise may contribute to an attenuation of oxygen-dependent neutrophil killing.

## 213. Mackinnon, L.T., T.W. Chick,

**A. van As, and T.B. Tomasi:**

Decreased levels of secretory immunoglobulins following prolonged exercise.

*Medicine and Science in Sports and Exercise* 18:S40, 1986.

### Authors' abstract

A previous study from this lab (Tomasi et al., J.Clin. Immunol. 1982, 2:173) showed that secretory IgA decreases immediately after a two hour exercise. The

purpose of the present study was to follow the time course of the mucosal immune response to prolonged exercise. Six male competitive bicyclists rode a bicycle ergometer for two hours at 90% of anaerobic threshold. Parotid saliva was sampled at four times: immediately before, and immediately, 1 and 24 hours after exercise. Immunoglobulins (Ig) were measured by direct competitive ELISA. Both IgA and IgM levels decreased after exercise (63% and 55% decreases, respectively;  $P < 0.01$ ), remained low for one hour, and returned to pre-exercise levels by 24 hours. Salivary IgG and serum IgA, IgG and IgM levels did not change, indicating a specific effect on secretory Ig. These data show that the mucosal immune system is suppressed by prolonged exercise, and suggest that an athlete may be susceptible to upper respiratory infection after intense exercise. To determine if prolonged exercise alters other immune parameters, natural killer (NK) activity was measured by  $^{51}\text{Cr}$  release in peripheral blood lymphocytes taken at the four times. NK activity did not change immediately after, but was suppressed one hour after exercise (35% decrease;  $P < 0.01$ ), and returned to pre-exercise levels by 24 hours. These data show that prolonged intense exercise suppresses parameters of both systemic and mucosal immunity, and that the time course of suppression varies between parameters.

## 214. Mackinnon, L.T., T.W. Chick,

**A. Van As, and T.B. Tomasi:**

The effect of exercise on secretory and natural immunity.

*Advances in Experimental Medicine and Biology* 216A:869-876, 1987.

### Authors' abstract

Secretory immunity—intense endurance exercise suppresses salivary immunoglobulins. The exercise-induced decrease is specific for the secretory antibodies IgA and IgM. The suppression of secretory Ig is transitory, lasting at least one hour, and returning to pre-exercise levels by 24 hours after a single bout of severe exercise. These results suggest that anecdotal statements by athletes and their coaches of an increased susceptibility to upper respiratory infection after severe exercise could be related to changes in secretory immunity.

Natural immunity—Natural killer activity of PBL is suppressed one hour after intense endurance exercise. This effect is transitory, since activity returns to pre-exercise levels by 24 hours after a single bout of exercise. The decrease in NK lytic activity is due to a decrease in the percentage of NK cells (Leu-11a+ cells). When NK cell activity is expressed on a per cell basis, it appears that activity is enhanced after exercise. These results indicate

that prolonged intense exercise alters parameters of both mucosal and natural immunity, and suggest that severe exercise may be a form of stress associated with changes in immune reactivity.

**215. Mackinnon, L.T., T.W. Chick,**

**A. Van As, and T.B. Tomasi:**

Effects of prolonged intense exercise on natural killer cell number and function.

In: *Exercise Physiology: Current Selected Research*, vol. 3, edited by C.O. Dotson, and J.H. Humphrey. New York: AMS Press, 1986. p.77-89.

**Authors' abstract**

Natural killer (NK) cells are a lymphocyte cell population capable of recognizing and killing certain tumor cells and virally infected cells. Stress is a well-known suppressor of NK activity. The purpose of this project was to study the effects of a physical stress, intense endurance exercise, on NK activity and cell number. Seven competitive cyclists rode a bicycle ergometer for 2 hours at 90% of anaerobic threshold. Venous blood was sampled at four times: immediately before and after exercise, and 1 and 24 hours postexercise. Total NK activity, measured by  $^{51}\text{Cr}$  release, was unchanged immediately after, but decreased 24% 1 hour after exercise ( $P < 0.01$ ) and returned to preexercise levels by 24 hours. Flow cytometry showed a 50% decrease in the percentage of lymphocytes exhibiting the NK marker Leu11 ( $P < 0.025$ ). When cytotoxic activity is expressed on a per cell basis to adjust for these changes in cell number, cytotoxic activity actually increased 40% at both times after exercise, suggesting a possible activation of killing. Catecholamines and B-endorphin stimulate NK activity. Blood levels of these hormones increased dramatically after exercise, suggesting a possible role for these molecules in augmenting NK activity during and after exercise. These data suggest that intense exercise may stimulate natural immunity.

**216. MacNeil, B., L. Hoffman-Goetz,**

**A. Kendall, and Y. Arumugam:**

Acute exercise and blood lymphocyte function in man.

*FASEB Journal* 4:A863, 1990.

**Authors' abstract**

The purpose of this study was to investigate the effects of intensity and duration of exercise on immunological function in men of defined fitness groups. Three fitness groups participated in the study: low (LF;  $\text{VO}_2\text{max} = 44.9 \pm 1.5$  ml  $\text{O}_2/\text{kg}/\text{min}$ ), moderate (MF;  $\text{VO}_2\text{max} = 55.2 \pm 1.6$  ml  $\text{O}_2/\text{kg}/\text{min}$ ), high (HF;

$\text{VO}_2\text{max} = 63.3 \pm 1.8$  ml  $\text{O}_2/\text{kg}/\text{min}$ ) and a mixed control group (C;  $\text{VO}_2\text{max} = 52.4 \pm 2.3$  ml  $\text{O}_2/\text{kg}/\text{min}$ ). Subjects completed four randomly ordered cycle ergometer rides: Ride 1; 30 min at 65%  $\text{VO}_2\text{max}$ , Ride 2; 60 min at 30%  $\text{VO}_2\text{max}$ , Ride 3; 60 min at 75%  $\text{VO}_2\text{max}$  and Ride 4; 120 min at 65%  $\text{VO}_2\text{max}$ . Blood samples were obtained at various times before and after the exercise sessions. Lymphocyte responses to the T cell mitogen Concanavalin A (Con A) were determined at each time sample through the incorporation of radio-labeled thymidine ( $^3\text{H}$  TdR). Data reveal that the exercising groups had a lower average uptake of ( $^3\text{H}$  TdR) than the control group with the LF group having the lowest overall response. The greatest reduction in uptake occurred two hours after the exercise bout in all groups. Increasing the intensity of exercise (Ride 2 Vs. Ride 3) resulted in greater reductions in ( $^3\text{H}$  TdR) uptake, seen two hours after exercise, with the largest reductions present in the HF group. Longer durations of activity (Ride 1 vs Ride 4) did not further reduce the proliferation response (uptake of  $^3\text{H}$  TdR) two hours after exercise irrespective of group. This study shows that immune function is transiently reduced two hours after exercise to an extent dependent on the intensity of activity. The results suggest that although LF subjects may have a lower baseline response, they are less affected by an acute bout of high intensity exercise. Conversely, the HF group displayed greater responses overall but were more severely affected by high intensity exercise.

**217. MacNeil, B., L. Hoffman-Goetz,**

**A. Kendall, M. Houston, and**

**Y. Arumugam:**

Lymphocyte proliferation responses after exercise in men: fitness, intensity, and duration effects.

*Journal of Applied Physiology* 70:179-185, 1991.

**Authors' abstract**

This study investigated the effects of intensity and duration of exercise on lymphocyte proliferation as a measure of immunologic function in men of defined fitness. Three fitness groups—low (maximal  $\text{O}_2$  uptake, or  $\text{VO}_2\text{max} = 44.9 \pm 1.5$  ml  $\text{O}_2/\text{kg}/\text{min}$  and sedentary), moderate ( $\text{VO}_2\text{max} = 55.2 \pm 1.6$  ml  $\text{O}_2/\text{kg}/\text{min}$  and recreationally active), and high ( $\text{VO}_2\text{max} = 63.3 \pm 1.8$  ml  $\text{O}_2/\text{kg}/\text{min}$  and endurance trained)—and a mixed control group ( $\text{VO}_2\text{max} = 52.4 \pm 2.3$  ml  $\text{O}_2/\text{kg}/\text{min}$ ) participated in the study. Subjects completed four randomly ordered cycle ergometer rides; ride 1, 30 min at 65%  $\text{VO}_2\text{max}$ ; ride 2, 60 min at 30%  $\text{VO}_2\text{max}$ ; ride 3, 60 min at 75%  $\text{VO}_2\text{max}$ ; and ride 4, 120 min at 65%  $\text{VO}_2\text{max}$ . Blood samples were obtained at various times before and after the exercise sessions.

Lymphocyte responses to the T cell mitogen concanavalin A were determined at each sample time through the incorporation of radiolabelled thymidine ( $^3\text{H}$  TdR). Despite differences in resting levels of ( $^3\text{H}$ ) TdR uptake, a consistent depression in mitogenesis was present 2 h after an exercise bout in all fitness groups. The magnitude of the reduction in T cell mitogenesis was not affected by an increase in exercise duration. A trend toward greater reduction was present in the highly fit group when exercise intensity was increased. The reduction in lymphocyte proliferation to the concanavalin A mitogen after exercise was a short-term phenomenon with recovery to resting (preexercise) values 24 h after cessation of the work bout. These data suggest that single sessions of submaximal exercise transiently reduce lymphocyte function in men and that this effect occurs irrespective of subject fitness level.

**218. Mahan, M.P. and M.R. Young:**

Immune parameters of untrained or exercise-trained rats after exhaustive exercise.

*Journal of Applied Physiology* 66:282-287, 1989.

**Authors' abstract**

The effect of a single exhaustive swimming exercise bout on immune competence of untrained or exercise-trained female Wistar rats was compared with the competence of control sedentary rats. After the exhaustive exercise bout, the blastogenic response to concanavalin A by spleen cells of untrained rats was extensively suppressed, whereas the response of the trained rats was only marginally suppressed. The suppressed immune competence of the untrained rats after the exhaustive exercise was associated with an increase in immune-suppressive activity of splenic lymphocytes. The macrophages of the untrained rats and of the control sedentary rats were slightly immune suppressive to normal spleen cells through a prostaglandin-dependent mechanism. The addition of prostaglandin  $\text{E}_2$  ( $\text{PGE}_2$ ) to the blastogenesis cultures revealed that the spleen cells of untrained rats were usually sensitive to the suppressive effects of  $\text{PGE}_2$ . In contrast to the untrained rats, the marginal level of the immune suppression trained rats after the exhaustive exercise was associated with a lesser degree of lymphocyte-suppressive activity, an immune stimulatory activity by the splenic macrophages, and an insensitivity of the splenic lymphocytes to the suppressive effects of  $\text{PGE}_2$ .

**219. Maidorn, V.K.:**

Die Bedeutung des Immunsystems für die Infektanfälligkeit bei Sportlern.  
*Sportarzt und Sportmedizin* 7:143-145, 1974.

**Author's abstract**

Relying on contemporary information on the human system of immunity, the antibody deficiency syndrome is under discussion as being the cause of the tendency to infection amongst sportsmen. Experience with gamma globulin substitution has shown that it is to be recommended as a prophylactic in cases of tendency to infection.

**220. Maisel, A.S., T. Harris, C.A. Rearden, and M.C. Michel:**

$\beta$ -adrenergic receptors in lymphocyte subsets after exercise. Alterations in normal individuals and patients with congestive heart failure.  
*Circulation* 82:2003-2010, 1990.

**Authors' abstract**

Dynamic exercise increases the number of  $\beta$ -adrenergic receptors in mixed lymphocytes by a mechanism that is incompletely understood. In a set of in vivo studies, we have investigated the effects of dynamic exercise on the subset distribution of circulating lymphocytes and on the number of  $\beta$ -adrenergic receptors in each of these subsets in two groups of patients. In healthy subjects, exercise increased plasma norepinephrine and epinephrine and caused lymphocytosis. Whereas the number of  $\text{T}_{\text{H}}$  helper cells increased only modestly, the number of  $\text{T}_{\text{S}}$  suppressor/cytotoxic and natural killer cells more than tripled. The number of  $\beta$ -adrenergic receptors varied among subsets but was not significantly altered by dynamic exercise in any subset except natural killer cells (35% increase,  $p = 0.0302$ ). In a group of patients with congestive heart failure, dynamic exercise increased plasma norepinephrine but did not alter plasma epinephrine and did not cause significant lymphocytosis. We did not detect any significant alterations of circulating leukocyte subsets or  $\beta$ -adrenergic receptors in any of these subsets after exercise. A combined analysis of healthy patients and heart failure patients revealed a significant correlation between increases in plasma epinephrine and increases in circulating lymphocytes. We conclude that the exercise-induced increase in  $\beta$ -adrenergic receptors of mixed lymphocytes is predominately caused by a redistribution of circulating cell subsets that differ in their  $\beta$ -adrenergic receptor number. This appears to be mediated by epinephrine rather than norepinephrine.

**221. Maisel, A.S., K.U. Knowlton, P. Fowler, A. Rearden, M.G. Ziegler, H.J. Motulsky, P.A. Insel, and M.C. Michel:**

Adrenergic control of circulating lymphocytes subpopulations. Effects of congestive heart failure, dynamic exercise, and terbutaline treatment. *Journal of Clinical Investigation* 85:462-467, 1990.

**Authors' abstract**

The current studies were undertaken to explore the relationship between enhanced sympathetic nervous activity and lymphocyte subset distribution in three settings: congestive heart failure, dynamic exercise, and  $\beta$ -adrenergic agonist treatment. We compared the number and subset distribution of circulating lymphocytes in 36 patients with congestive heart failure and 31 age-matched control subjects. The number of circulating lymphocytes was lower in heart failure than in control. This was due to a reduction in  $T_{\text{suppressor/cytotoxic}}$  and natural killer cells without significant alteration of  $T_{\text{helper}}$  cells. The extent of the alteration was similar in patients with idiopathic and ischemic heart failure, but the reduction was more pronounced in patients with New York Heart Association class III-IV than in class I-II. The plasma catecholamine elevation in heart failure was also independent of etiology but more pronounced in the more severely ill patients. We also assessed lymphocyte subsets after acute stimulation of sympathetic activity by dynamic exercise and after treatment with the  $\beta$ -adrenergic agonist terbutaline. Dynamic exercise until exhaustion increased the number of circulating lymphocytes in healthy controls and heart failure patients in a subset-selective manner. By contrast, a 7-d treatment with terbutaline caused a reduction in the circulating number of lymphocytes in some subsets that was identical to that seen in heart failure patients. We conclude that prolonged sympathetic activity reduces the number of circulating lymphocytes by a  $\beta$ -adrenergic mechanism. Such alterations might be involved in the pathophysiology of heart failure and other disease states involving increased activity of the sympathetic nervous system.

**222. Mäki, T.:**

Density and functioning of human lymphocytic  $\beta$ -adrenergic receptors during prolonged physical exercise.

*Acta Physiologica Scandinavica* 136:569-574, 1989.

**Author's abstract**

In order to study the regulation of  $\beta$ -adrenergic receptor number and function in response to prolonged physical

effort, lymphocytic  $\beta$ -adrenoceptor density (determined by (-)[<sup>125</sup>I] iodocyanopindolol binding), lymphocytic basal and isoproterenol-stimulated cyclic AMP (cAMP) production and concentrations of plasma catecholamines were measured before and during 3 h running exercise in eight healthy volunteers. A significant ( $P < 0.01$ ) increase of the lymphocytic  $\beta$ -adrenoceptor density from  $45 \pm 4$  to  $81 \pm 9$  fmol/mg protein ( $X \pm \text{SEM}$ ) took place during the first hour of exercise. As the exercise was continued for up to 2.1-3 h, the receptor densities did not change significantly any more and remained elevated ( $72 \pm 9$  fmol/mg protein) in comparison to the resting levels ( $P < 0.02$ ). The isoproterenol-stimulated cAMP production of the lymphocytes increased during the first hour of running from  $190 \pm 36$  to  $269 \pm 56$  pmol/mg protein ( $P < 0.01$ ) and returned to the resting level at the end of the exercise ( $182 \pm 38$  pmol/mg protein). The mean levels of plasma catecholamines increased approximately sixfold during the first hour of exercise and remained elevated until the end of the running. This study demonstrates that the  $\beta$ -adrenergic receptor system is activated in lymphocytes during prolonged aerobic physical exercise. This activated state becomes, however, attenuated within 2-3 h of exercise as indicated by a diminishing ability of  $\beta$ -adrenoceptors to mediate catecholamine-induced cAMP production.

**223. Mark, D.A., D. Bovbjerg, H. Katzeff, R. Rivlin, and M.E. Weksler:**

Effects of voluntary exercise and caloric restriction on murine lymphocyte responses, thyroid hormone levels, and life span.

In: *Nutrition, Immunity, and Illness in the Elderly*, edited by R.R. Chandra. Oxford: Pergamon, 1985. p.192-199.

**Authors' abstract**

Underfeeding of rodents has been shown to enhance various immune reactions, prolong lifespan, and increase levels of physical activity. We have investigated the possibility that increased physical activity is the cause of the immunological and life span changes usually attributed to underfeeding. Mice running 3-4 kilometers per night were provided with free access to running wheels. In a longevity study, exercising mice of the short-lived autoimmune strain MRL/lpr tended to live longer than mice housed without voluntary access to running wheels. In a separate study, groups of male C57BL/6 mice were either underfed by 12% or exercised (allowed unlimited access to running wheels), underfed and exercised, or subjected to neither condition for three weeks. Exercise and underfeeding had opposite effects on splenic proliferative responses to the mitogens

phytohemagglutinin, concanavalin A, and *E. coli* lipopolysaccharide, and on serum levels of the thyroid hormones triiodothyronine and thyroxine. These results suggest that while exercise may influence immune responses and life span, increased physical activity is not likely to be the sole mediator of the immunomodulatory effects attributed to underfeeding.

#### 224. Martin, H.E.:

Physiological leukocytosis. The variation in the leukocyte count during rest and exercise, and after the hypodermic injection of adrenaline.  
*Journal of Physiology (London)* 75:113-129, 1932.

##### Author's abstract

1. The diurnal variation of the leukocyte count during rest has been examined and it has been shown: a) that the counts are steadiest and at a minimum when the subject's condition approximates most nearly to that of absolute physiological rest; b) that they rise with increase in the mental and physical activity of the subject, and c) that they tend to rise in the late afternoon and early evening, this being regarded as the period of greatest activity.

2. The effect of exercise on the peripheral blood was investigated. The total leukocyte count exhibited a rise varying from 15 to 48 p.c. of the resting value, and it returned to normal after about 30 min. rest. Further exercise then produced another rise in the count similar in type and degree to the first. The rise in total count was due to an increase in the number of all types of cell, but the lymphocytes showed the greatest increase.

3. The hypodermic injection of adrenaline is followed by a leukocytosis in which all types of cell showed an increase, but that of the lymphocytes is most marked. It is similar to the leukocytosis following exercise, and the theory has been advanced that the latter is produced by autogenously secreted adrenaline. The cells which cause the leukocytosis arise from two sources. The lymphocytes are in all probability derived from the lymph glands which contract under the influence of the adrenaline, and the granular cells are washed out of the bone marrow by the increased blood flow due to cardiac stimulation by the adrenaline.

#### 225. Masuhara, M., K. Kami, K. Umebayasi, and N. Tatsumi:

Influences of exercise on leukocyte count and size.  
*Journal of Sports Medicine* 27:285-290, 1987.

##### Authors' abstract

The effects of strenuous exercise performed by young athletes under defined conditions on white cell parameters was studied using a bicycle ergometer. The exercise caused remarkable increase in leukocyte counts, which was due to lymphocyte increase. A high correlation was seen between the increase in lymphocyte % and the maximum oxygen uptake. The increase in lymphocyte % was also correlated with the increase in epinephrine level. The exercise caused an increase in OKT8 and OKT9, OKB2 and OKB7 cells, and a decrease in ratio of OKT4/OKT8.

#### 226. Maulitz, R.M, D.S. Pratt, and

##### A.L. Schocket:

Exercised-induced anaphylactic reaction to shellfish.  
*Journal of Allergy and Clinical Immunology* 63:433-434, 1979.

##### Authors' abstract

The syndrome of immediate type I food hypersensitivity, mediated by tissue-bound IgE antibody and mast cell histamine release, is well recorded in the medical literature. This case study represents a previously undescribed late food hypersensitivity, induced only by strenuous exercise. Identification of this new syndrome illustrates classical epidemiologic analysis, improves medical advice for the allergic and athletically inclined, and raises new questions in the areas of allergy and immunology.

#### 227. McCarthy, D.A. and M.M. Dale:

The leukocytosis of exercise. A review and model.  
*Sports Medicine* 6:333-363, 1988.

##### Authors' abstract

Exercise is known to induce an immediate leukocytosis, the magnitude of which is related, in most instances, to the intensity and duration of the work. On finishing exercise however, the leukocyte count may change in any one of several different ways. The pattern of post-exercise changes in the leukocyte count is determined mainly by the time which has elapsed since beginning exercise, rather than the work intensity or the total work done if, for example, exercise has been intermittent. Consideration of, firstly, the circumstances under which the plasma concentrations of catecholamines and cortisol have been

found separately to correlate with the leukocyte count at the finish of exercise, and, secondly, the effects on the leukocyte count of exogenous administration of these substances has led us to develop a model which can satisfactorily account for all of the principal changes in the leukocyte count that have been noted during and after exercise. It is proposed that catecholamines produced during exercise act to increase the ratio of circulating to non-circulating leukocytes, while cortisol acts, by a mechanism which involves a time lag increase in the total number of leukocytes in the vascular compartment. Examination of previously published reports shows that many contain results which support this model. Using the model as a basis, some predictions are made that can be tested experimentally and some experiments are suggested which should help elucidate the mode of action of catecholamines and cortisol.

**228. McCarthy, D.A., J.D. Perry,**

**R.D. Melsom, and M.M. Dale:**

Leukocytosis induced by exercise.

*British Medical Journal* 295:636, 1987.

#### Authors' abstract

We studied 10 healthy white men (mean age 42.5, range 26-52) who continued their usual daily routine for 24 hours before the study but avoided strenuous exercise. For the study, each man exercised at a rate close to his maximum for 30 minutes between 1000 and 1100, swimming about 1 km, playing squash, or jogging roughly 6 km (13 sessions altogether—five jogging, four

squash, and four swimming): nine men did one each and one did four. Blood samples were taken immediately before and after exercise and at intervals over the next five and a half hours. Control samples were taken at similar times during a normal working (control) day. Leukocyte counts were measured by routine procedures. Counts in control samples were within the normal range except for one that was slightly low. During the control day leukocyte numbers increased slightly (table).

Immediately after 30 minutes' exercise the mean leukocyte count had risen to 115%, but by one hour it had fallen to 104% compared with mean control counts (= 100%). These mean values, however, hid considerable individual variation. In eight subjects exercise caused a small immediate increase in leukocyte numbers; at one hour the count had fallen to baseline in four men but remained the same or had even increased in the others.

The two other subjects had an immediate slight decrease in leukocyte numbers, which persisted until one hour.

Irrespective of the immediate effect a delayed and

prolonged leukocytosis that reached a peak between two and four hours was noted in all subjects; this was

predominantly due to a rise in neutrophils. The leukocyte count did not exceed the upper limit of normal immediately after exercise in any of the subjects, but it did so

during the delayed leukocytosis in six of the 13 sessions (done by four of the ten subjects). The magnitude of the delayed leukocytosis (mean 175%,  $n = 13$ ) varied greatly among subjects (range 112-235%) when compared with control values before exercise (= 100%). It was unrelated to the type of exercise but was most pronounced in subjects who took a little or no regular exercise.

**Effect of half an hour of exercise on leukocyte count ( $\times 10^9/l$ ). Results are the means of 13 experiments (SD)**

	Baseline	Time (h) after start of exercise			
		1	2.75	4.5	6
Exercise	5.97 (2.02)*‡	6.97 (1.74)	10.45 (3.27)*†	10.00 (3.05)	8.83 (2.67)
Control Period †	6.68 (1.52)	6.73 (1.50)	6.83 (1.47)†	7.02 (1.36)	7.19 (1.55)

By paired t tests the difference between these two counts was significant: \* $P < 0.01$ ; † $P < 0.01$ ; ‡ $P < 0.05$ . † Random activity.

**229. Megyesi, Z., Gy. Cseh, and J. Csengody:**

L'effet du travail sur le taux de properdine du sérum sanguin.

*Revue de Aggressologie* 2:359-362, 1962.

**Authors' abstract**

According to the examinations we carried out on sportsmen, the activity of properdine in the blood serum shows a small increase after a moderate effort. After an extenuating work this activity diminishes in a very marked way, the intensity of the last largely surpassing that of the first. Reference is made to the importance of these phenomena as far as natural, specific resistance against infection is concerned.

**230. Meyer, M.H. and G. Pella:**

The effect of hard laboratory exercise on the total and differential leukocyte count of young women.  
*Research Quarterly* 18:271-278, 1974.

**Synopsis**

**Purpose.** To observe the effects of hard laboratory exercise on the total and differential white blood count of normal, young, adult women.

**Methods**

1. Subjects reported to the lab in a post-absorptive state or after a light lunch.
2. They reclined for 60 minutes in a quiet, darkened room, when blood samples and smears were taken at 30-minute intervals, and radial pulse rates were recorded at 5-minute intervals.
3. After stabilization, the subjects exercised on the electrodynamic brake bicycle ergometer at a rate of 0.162 horse power for a maximum of 15 minutes.
4. Heart rates were taken by precordial auscultation every 5 minutes.
5. Immediately after exercise the subjects again reclined for 90 minutes when blood samples, smears, and heart rates were taken at 30-minute intervals.

**Results**

1. The maximum increase of total leukocyte count was found in the first post-exercise sample.
2. In all but 2 cases, the 30-minute post-exercise sample showed a definite decrease in total leukocyte count.
3. Lymphocyte counts showed an immediate post-exercise rise of 21.1% followed by a decrease.

4. The neutrophils showed an immediate post-exercise decrease of 15.4% followed by a rise of 0.5%.

5. Post-exercise leukocytosis is repeatable and may be followed by neutrophil leukopenia.

**Conclusions**

1. Hard laboratory exercise of short duration produces leukocytosis in normal, young, adult women.

2. The mechanism of exercise leukopenia is unknown.

**231. Michna, H., G. Hartmann, and W. Schänzer:**

Morphological, biochemical and immunological studies of an autonomic regulation of peritoneal macrophage activity during a simulated aerobic endurance training.

*International Journal of Sports Medicine* 8:157, 1987.

**Authors' abstract**

Mice were subjected to daily treadmill exercise over 3 weeks with a view to characterizing the reactions of peritoneal macrophages and intracardiac autonomic nervous system to aerobic endurance training (Tittel and Otto, 1970). The results obtained concurrently indicated an increased capacity of the macrophages for chemotaxis, migration and phagocytosis after treadmill training. The fact that the noradrenaline concentration in the ventricular myocardium remains unchanged at this time casts doubt on the assumption of an autonomic regulation of macrophage activity. Since the reduced area of fluorescent nerve fibers in the ventricular myocardium suggests an increased axonal degeneration, the increased macrophage activity may be assumed to be due to possible chemotactic signals associated with axonal degeneration in the ventricular myocardium. This would also be in accordance with our electron microscopic findings obtained in the ventricular myocardium under training conditions.

**232. Middeke, M., J. Remien, and**

**H. Holzgreve:**

The influence of sex, age, blood pressure and physical stress on  $\beta_2$ -adrenoceptor density of mononuclear cells.

*Journal of Hypertension* 2:261-264, 1984.

**Authors' abstract**

The influence of sex, age, blood pressure and physical stress on  $\beta_2$ -adrenoceptor density on intact mononuclear cells was investigated in normotensives and

in patients with essential hypertension using ( $\pm$ )125-iodocyanopindolol as radio-ligand. The intra-individual receptor status under basal conditions at rest was fairly constant. The mean individual deviation of  $\beta_2$ -adrenoceptor density was 11% after a time period of 3  $\pm$  1.9 months. The receptor number increased with age: there was a positive correlation ( $r = 0.59$ ) between age and  $\beta_2$ -adrenoceptor density. No significant difference existed between men and women matched for age and mean arterial blood pressure ( $548 \pm 179$  versus  $481 \pm 246$  maximal binding sites per cell). A highly significant positive correlation ( $r = 0.73$ ) existed between the mean arterial blood pressure and the  $\beta_2$ -adrenoceptor density over a wide range of normal and increased blood pressure. A factorial analysis revealed a significant correlation between mean arterial pressure and  $\beta_2$ -adrenoceptor density, but not between age or sex and  $\beta_2$ -adrenoceptors followed by a fall to or even below the starting values after 15-30 min rest. Physical stress led within 15 min to a significant increase in  $\beta_2$ -adrenoceptors followed by a fall to or even below the starting values after 15 to 30 min rest. It is concluded that  $\beta_2$ -adrenoceptor density on intact mononuclear cells correlates significantly with mean arterial blood pressure and with age. However, factorial analysis revealed a significant positive correlation only between mean arterial blood pressure and the receptor number but not between age and the receptor number. Sex has no significant influence on the receptor density. The observed rapid increase of  $\beta_2$ -adrenoceptors under physical stress is possibly due to an acute activation of preformed inactive  $\beta_2$ -binding sites.

### 223. Midtvedt, T. and K. Midtvedt:

Sport and infection.

*Scandinavian Journal of Social Medicine*  
Suppl.22:241-244, 1982.

#### Authors' abstract

Infectious diseases are apparently as common among athletes as among the average population. An infection will normally lead to decreased performance, i.e., an athlete will "feel" an infection more than a non-athletic individual. Some infections are, however, more common among athletes. These are often related to the kind of athletic performance and the kind of training methods involved but can usually be prevented. In many areas there is a lack of knowledge and the need for more research is underlined.

### 234. Mochhala, S.M., K.P. Fung, R. Yuen, and N.P. Das:

Effects of acute physical exercise on aryl hydrocarbon hydroxylase activity in human peripheral lymphocytes.  
*Life Sciences* 47:427-432, 1990.

#### Authors' abstract

It has been reported that physical exercise may enhance cytochrome P-450 dependent drug metabolism *in vivo*. In this study we report that the specific activity of aryl hydrocarbon hydroxylase (AHH) in human peripheral lymphocytes (HPL) is enhanced approximately two-fold following acute physical exercise. This enhancement of AHH activity in HPL appears to be strongly correlated with enhanced lymphocyte count as well as induced metabolic and exercise stress but not with the intrinsic physical fitness of individuals.

### 235. Moorthy, A.V. and S.W. Zimmerman:

Human leukocyte response to an endurance race.  
*European Journal of Applied Physiology* 38:271-276, 1978.

#### Authors' abstract

The response of circulating leukocytes (WBC's) with regard to changes in number, proportion of neutrophils versus lymphocytes and changes in lymphocyte function as well as proportions of T and B cells was studied in eleven men who ran a 20 mile race. A marked leukocytosis was noted 10-15 min after the race with the predominant increase being polymorphonuclear leukocytes ( $P < 0.001$ ). A significant rise in mean serum cortisol levels was also noted ( $P < 0.001$ ) which correlated with both the increase in total WBCs ( $P < 0.001$ ) and granulocytes ( $P < 0.001$ ), but not lymphocytes. The increase in serum cortisol was inversely correlated with miles of prior training ( $P < 0.001$ ). An increase in lymphocytes from  $1767 \pm 112/\text{mm}^3$  to  $2431 \pm 202/\text{mm}^3$  was less than previously described in short-term exercise. As with short-term exercise the most significant increase in lymphocytes was in "B" lymphocytes bearing surface immunoglobulin ( $P < 0.0025$ ). However, in contrast to short-term exercise, lymphocytes maintained good *in vitro* response to the mitogen phytohemagglutinin. This study demonstrates that endurance racing produces a more marked granulocytosis and less lymphocytosis than short bouts of exercise. It is suggested that the degree of leukocytosis is stress dependent in that it was positively correlated with serum cortisol and inversely correlated with prior training.



- 236. Morgan, B.B., Jr., G.D. Coates, and E.A. Alluisi:**

Effects of illness (*Phlebotomus* fever) on sustained performance and muscular output.  
*Human Factors* 15(1):53-65, 1973.

**Authors' abstract**

During a period of illness with *Phlebotomus* fever, decrements in the performance of eight experimental subjects were found to be approximately 18% in average work efficiency (sustained performance) and 14% in average muscular output. Both aspects of performance had recovered completely four days after the day of peak illness. Analyses of 24 biomedical indices of infection were also computed, and the average biomedical response was found to have decreased approximately 26% during illness without recovery to normal levels at the end of the 15-day study.

- 237. Morse, L.J., J.A. Bryan, J.P. Hurley, J.F. Murphy, T.F. O'Brien, and W.E.C. Wacker:**

The Holy Cross College football team hepatitis outbreak.  
*Journal of the American Medical Association* 219:706-708, 1972.

**Authors' abstract**

During a 15-day period in September and October 1969, an outbreak of infectious hepatitis affected the members of a college football team. Of 97 persons exposed, 90 were infected, 32 experienced typical icteric disease, 22 were anicteric but symptomatic, and 36 asymptomatic players were recognized as having significantly elevated serum glutamic pyruvic transaminase values (>100 units). Other athletes, using the same facilities but arriving six days after the established date of exposure, were unaffected. The decision to obtain blood samples from the entire team, as soon as the original cases were recognized, resulted in the demonstration of an unexpectedly high attack rate of 93%. Epidemiologic investigation revealed that an infected group of children in the neighborhood, an imperfect drinking water supply, a warm August day, a football team in training, and a local fire were links in the chain which resulted in this most unusual outbreak of infectious hepatitis.

- 238. Muir, A.L., M. Cruz, B.A. Martin, H. Thommasen, A. Belzberg, and J.C. Hogg:**

Leukocyte kinetics in the human being: role of exercise and catecholamines.  
*Journal of Applied Physiology* 57:711-719, 1984.

**Authors' abstract**

In six normal supine subjects epinephrine infusion produced a greater leukocytosis with smaller changes in heart rate and blood pressure than did norepinephrine or isoproterenol. Upright exercise in those subjects produced a greater leukocytosis than supine exercise at the same work load. To determine the lung's participation in these events, indium-labeled neutrophils (PMN) were given to four of the subjects. We found that 20-25% were retained in the first pass through the lung when compared with technetium-labeled erythrocytes. The number of labeled PMN in the lung gradually decreased and the number in the spleen and liver increased. Exercise and catecholamine infusion caused an acceleration in the release of labeled cells from the lung, an increase in both labeled and unlabeled cells in the peripheral blood, and an increase in the number of labeled cells in the liver and spleen. This suggests that increased perfusion of low-flow areas in the lung may contribute to the increased leukocytosis seen in association with both exercise and catecholamine infusion.

- 239. Mulligan, S.P., E.J. Wills, and G.A.R. Young:**

Exercise-induced CD8 lymphocytosis: a phenomenon associated with large granular lymphocyte leukaemia.  
*British Journal of Haematology* 75:175-180, 1990.

**Authors' abstract**

This report describes a patient with a large granular lymphocyte leukaemia (CD8+ lymphoproliferative disease) and a severe neutropenia ( $<0.5 \times 10^9/l.$ ) in whom exercise resulted in a marked lymphocytosis, a phenomenon which has not previously been recorded. The lymphocyte count at rest was within normal limits ( $2.2 \times 10^9/l.$ ), rose to a peak with strenuous exercise ( $38 \times 10^9/l.$ ), then fell to the resting level within 15 min of cessation of exercise. The peripheral blood mononuclear cells showed the morphology of large granular lymphocytes (LGL) by light and electron microscopy both at rest (30%) and to a much greater extent during exercise (70%). Immunophenotyping of these lymphocytes during exercise demonstrated that the predominant cell was CD3+, CD8+, CD57+ (Leu 7)/CD4-, CD16, CD25. In the resting state, despite a total lymphocyte count within the

normal range, surface marker studies indicated an excess of cells with the CD8+/CD57 + T cell phenotype (26%; cf. normal range  $\leq 10\%$ ). Functional assays revealed a minimal increase in natural killer (NK) activity during exercise. T cell receptor  $\beta$  chain gene rearrangement was demonstrable in the peripheral blood at rest and during exercise. Although severe neutropenia was present, the growth of normal colony forming units, granulocyte-macrophage (CFU-GM), was not inhibited by patient lymphocytes and no anti-neutrophil antibodies were demonstrated. Finally, hyposplenism has developed and the relationship of this to the LGL leukaemia is discussed. In summary, the findings demonstrated large granular lymphocyte leukaemia as the primary disorder for which the primary manifestation, apart from the neutropenia, was a marked exercise-induced lymphocytosis.

**240. Müns, G., H. Liesen, H. Riedel, and K.-Ch. Bergmann:**

Einfluss von Langstreckenlauf auf den IgA-Gehalt in Nasensekret und Speichel.

*Deutsche Zeitschrift für Sportmedizin* 40:63-65, 1989.

**Author's abstract**

The stress-related changes in the IgA concentrations in nasal secretion and saliva were tested in 15 male participants in a marathon race (age  $36 \pm 11.5$  years, 4 mmol/l lactate threshold  $4.45 \pm 0.28$  m/s) and in 33 male entrants in an 31 km race (age  $49.3 \pm 5.5$  years,  $4.01 \pm 0.39$  m/s). Both races led to significant reductions in the IgA concentrations both in the nasal secretion in the saliva. While the IgA values were still significantly lower 18 hours after the 31 km race, they returned to their original level three days later.

**241. Naesh, O., I. Hindberg, J. Trap-Jensen, and J.O. Lund:**

Post-exercise platelet activation-aggregation and release in relation to dynamic exercise.

*Clinical Physiology* 10:221-230, 1990.

**Authors' abstract**

Relatively scarce information is found on the period immediately following physical stress, with special reference to human platelet activity. This, in connection with earlier observations of an increase in platelet release products and hyperaggregation in eight healthy non-medicated volunteers during and 1 h after cycle exercise of submaximal intensity. ADP-induced platelet aggregability was enhanced in the last minute of exercise followed by a decreased aggregability 1 h after. Adrenalin-

induced platelet aggregation showed the same attenuation after exercise but no change during work. The release products  $\beta$ -thromboglobulin and serotonin ion plasma showed significant increases after exercise. This is taken as evidence of an enhanced platelet activity following exercise. A normal stress-response, measured as increase in cyclic AMP in plasma, was observed. In conclusion, platelets are activated following moderate exercise and it seems valid to include the post-exercise period in future studies.

**242. Nehlsen-Cannarella, S.L., D.C. Nieman, A.J. Balk-Lamberton, P.A. Markoff, D.B.W. Chritton, G. Gusewitch, and J.W. Lee:**

The effects of moderate exercise training on immune response.

*Medicine and Science in Sports and Exercise* 23:64-70, 1991.

**Authors' abstract**

The relationship between moderate exercise training (ET) (five 45-min sessions per week, brisk walking at 60% heart rate reserve for 15 wk) and changes in immune system variables and function was investigated in a group of 36 sedentary, mildly obese women. The study was conducted using a two (exercise (EX) and nonexercise (NEX) groups) by three (baseline, 6 wk, 15 wk testing session) factorial design, with data analyzed using repeated measures ANOVA. The pattern of change over time between groups for number of peripheral blood lymphocytes (total), T cells (CD5), B cells (CD20), and serum IgG, IgA, and IgM levels was significantly different. This was not the case for spontaneous blastogenesis or number of T helper/inducer cells (CD4) or T cytotoxic/ suppressor cells (CD8). Within-EX-group changes were characterized by significant decreases in percentages and number of total lymphocytes, and in T cell number after 6 wk, and significant increases in each of the serum immunoglobulins after both 6 and 15 wk of training. B cell number increased significantly in NEX subjects relative to baseline values at both 6 and 15 wk, with no significant changes experienced in EX subjects. In summary, these data suggest that moderate ET is not associated with an improvement in lymphocyte function but is associated with a 20% increase in serum immunoglobulins and several small changes in circulating numbers of immune system variables, highlighted by significant decreases in circulating numbers of lymphocytes, particularly the T cell subpopulation. These changes were especially apparent after 6 wk of training, with some attenuation by 15 wk.

**243. Nehlsen-Cannarella, S.L., D.C. Nieman,**

**J. Jessen, L. Chang, G. Gusewitch,**

**G.G. Blix, and E. Ashley:**

The effects of acute moderate exercise on lymphocyte function and serum immunoglobulin levels.

*International Journal of Sports Medicine*

12:391-398, 1991.

**Authors' abstract**

The extent and duration of changes on lymphocyte function and serum immunoglobulin (Ig) levels were examined in 12 women who walked 45 min at 60%  $\dot{V}O_2$  max in a laboratory setting. A 2-factor,  $2 \times 6$  design with repeated measures on both factors was utilized. The first factor was condition (exercise and rest), and the second factor was time (six times of measurement over a 24-h period), with treatment order counterbalanced. The 45-min walk, in comparison to rest in a seated position, was not associated with significant changes in circulating numbers of interleukin-2-activated T cells (CD5 and CD25) or on spontaneous or concanavalin-A-stimulated lymphocyte proliferation. A trend for decreased phytohemagglutinin-stimulated lymphocyte proliferation in comparison to the rest condition, however, was seen 1.5 h following the exercise bout ( $P = 0.047$ ). The patterns of change for serum IgG, IgA, and IgM were significantly different ( $P = 0.001$ ,  $P < 0.001$ ,  $P = 0.001$ , respectively) between conditions. IgG rose 7.2% immediately following exercise, and then returned to baseline 1.5 h later, which contrasted significantly with changes in the rest condition. These same patterns of change occurred also with IgA and IgM, but increases immediately following exercise were not significant, although a trend was seen for IgA ( $P = 0.03$ ). The 45-min walk had no effect on plasma cortisol and epinephrine levels relative to the rest condition, but was associated with a significant 89% increase in norepinephrine. These data suggest that moderate exercise leads to a transient increase in serum immunoglobulin levels by way of contribution from extravascular pools and/or nonspecific stimulation of memory B cells. Antigen-dependent mechanisms do not appear to play a major role.

**244. Neisler, H.M., M.H. Bean, J. Pittington,**

**W.R. Thompson, J.T. Johnson, and**

**J.L. Smith:**

Alteration of lymphocyte subsets and endocrine response during 42 days of competitive swim training.

*Medicine and Science in Sports and Exercise*

21:S110, 1989.

**Authors' abstract**

Seventeen male subjects ( $\bar{X}$  age =  $19.2 \pm 1.2$  yrs) were tested before (Pre) and within 5 minutes of completion (Post) of a typical swim workout at the beginning of the season and after 42 days of training. Training consisted of both swimming ( $\bar{X} = 49,000$  yds in 9 workouts/wk) and progressive weights ( $\bar{X} = 2$  sets/wk). Cortisol (Cort) and Growth Hormone (GH) were assayed by RIA. Thyroid Stimulating Hormone (TSH) and Prolactin (Pro) were assayed by EIA. Lymphocyte (LY) subsets were evaluated with two-color monoclonal antibodies for T4-T8, T3-I3, T11-B1, NKH1-T8, 2H4-T4 (Helper Inducer) and 4B4-T4 (Suppressor Inducer). All samples were assayed by the same technologists on the same instruments. A significant decrease in Pro and in T4, NK, 2H4-T4, 4B4-T4 and Helper/Suppressor ratio (H/S) ( $P < 0.002$ ) when expressed in absolute terms occurred between the two Pre sample times. Significant decreases in H/S, Cort, and Pro with an increase in GH ( $P < 0.0004$ ) occurred in both Pre to Post samples. Responses of LY, T8, NK, and TSH differed significantly between the two Pre to Post samples ( $P < 0.0001$ ). These data indicate that both chronic training and acute exercise can induce significant alterations in LY subsets as well as some pituitary hormones.

**245. Nelson, R.S., H. Sprinz,**

**J.W. Colbert, Jr., F.P. Cantrell,**

**W.P. Havens, Jr., and M. Knowlton:**

Effect of physical activity on recovery from hepatitis. *American Journal of Medicine* 16:780-789, 1954.

**Authors' abstract**

1. Eighty patients, presumably recovered from viral hepatitis, were re-examined twenty-two to thirty-three months later.
2. Although forty-six patients had symptoms, signs, or abnormalities of hepatic function, these alterations were mild and compatible with good health and full activity,
3. The lack of correlation between the occurrence of subjective and objective findings, as well as their mildness, made it impossible to assign them any clinical

significance. Biopsies made in forty of these patients revealed no evidence of significant scarring of the liver.

4. There was no apparent relationship between the original severity of hepatitis or the experiences of the patients in the intervening period and the findings at re-examination.

5. The failure to find any significant evidence of residual hepatic disease in these patients lends further support to the concept that activity far in excess of that usually prescribed in acute hepatitis did not inhibit sustained recovery in the patients described here.

#### **246. Nicholls, E.E. and R.A. Spaeth:**

The relation between fatigue and the susceptibility of guinea pigs to infections of Type I pneumococcus.  
*American Journal of Hygiene* 2:527-535, 1922.

##### **Synopsis**

**Purpose** To study the effects of physical exhaustion on susceptibility of guinea pigs to Type I pneumococcus.

##### **Methods**

1. Guinea pigs weighing between 150 and 300 grams were forced to run to exhaustion in motor-driven drums.
2. Each pig was subjected to 3 running periods and the injections of pneumococci were given either before or after running.

##### **Results**

1. In the unfatigued control group 80% of the animals died. In the animals fatigued 3 times before injection, 80% lived. In the animals fatigued 3 times after injection, 56% lived.

2. Albino guinea pigs were 30% more susceptible to pneumococci than pigmented pigs.

##### **Conclusions**

1. There is in guinea pigs a definite correlation between pigmentation and susceptibility to Type I pneumococcus.
2. Fatigue definitely increases the resistance of guinea pigs to lethal injections of Type I pneumococcus.

#### **247. Nieman, D.C., L.S. Berk,**

**M. Simpson-Westerberg, K. Arabatzis,  
W.S. Youngberg, S.A. Tan, J.W. Lee, and  
W.C. Eby:**

Effects of long-endurance running on immune system parameters and lymphocyte function in experienced marathoners.

*International Journal of Sports Medicine*  
10:317-323, 1989.

(Same as: Nieman, D.C., L.S. Berk,  
M. Simpson-Westerberg, K. Arabatzis,  
S. Youngberg, S.A. Tan, J.W. Lee, and W.C. Eby.  
The effects of long endurance running on immune system parameters and lymphocyte function in experienced marathoners.  
*Medicine and Science in Sports and Exercise*  
21:S109, 1989).

##### **Authors' abstract**

The extent and duration of changes in leukocyte subsets, lymphocyte subpopulations, spontaneous blastogenesis, cortisol, and catecholamines were measured in 10 experienced marathoners who ran 3-h to exhaustion in a laboratory setting. Blood samples were taken at baseline, 1-h of exercise, and 5-min, 1.5-h, 6-h, and 21-h recovery. The 3-h endurance run was associated with significant leukocytosis, granulocytosis, neutrophilia, monocytosis, and eosinopenia during recovery. All of these parameters except for eosinophils returned to normal by 2.1-h recovery. Total lymphocyte count increased 31% at 1-h exercise, then decreased by 19% at 1.5-h recovery when compared to baseline values. T-cell count showed no significant changes, but B-cell lymphocytosis was measured at 5-min and 6-h recovery.

T helper/T suppressor ratio (H/S) was significantly elevated 39% at both 1.5-h and 21-h recovery due to the decrease in number of T suppressor cells. Spontaneous blastogenesis was significantly increased 52% by 1-h exercise, and remained elevated throughout recovery. The increase in cortisol from baseline to 1.5-h recovery correlated positively with the increase in both total leukocyte count ( $r = 0.78$ ,  $P = 0.008$ ) and granulocyte count ( $r = 0.81$ ,  $P = 0.005$ ). Our results suggest that exhaustive endurance exercise in marathon runners is associated with many significant perturbations in immune system parameters, most of which return to normal levels by 21-h of recovery.

**248. Nieman, D.C., L.M. Johanssen, and J.W. Lee:**

Infectious episodes in runners before and after a roadrace.

*Journal of Sports Medicine and Physical Fitness* 29:289-296, 1989.

**Authors' abstract**

Various researchers have implied that regular and moderate exercise training may improve the ability of the immune system to protect the host from infection. In contrast, acute, maximal, and exhaustive exercise may have negative effects on the immune system. This study compared the incidence of infectious episodes in 273 runners during a two month training period prior to a 5K, 10K, or half-marathon race. In addition, the effect of the race experience on infectious episodes was studied. Twenty five per cent of the runners training more than 15 miles per week reported at least one infectious episode as compared with 34.3% of runners training less than 15 miles per week ( $P = 0.09$ ). Only 6.8% of the runners preparing for the half marathon race reported becoming sick with the flu versus 17.9% of the 5K and 10K runners ( $P = 0.067$ ). During the week following the roadrace, runners did not report an increase in infectious episodes as compared to the week prior to the race. These trends suggest that runners with a more serious commitment to regular exercise may experience less infectious episodes than recreational runners because of both direct and indirect effects on immunosurveillance. In addition, the stressful race experience does not appear to increase risk of acquiring an acute respiratory infection.

**249. Nieman, D.C., L.M. Johanssen, J.W. Lee, and K. Arabatzis:**

Infectious episodes in runners before and after the Los Angeles marathon (LAM).

*Journal of Sports Medicine and Physical Fitness* 30:316-328, 1990.

(Same as: Nieman, D.C., L.M. Johanssen, J.W. Lee, and K. Arabatzis. Infectious episodes in runners before and after the Los Angeles marathon.

*Medicine and Science in Sports and Exercise* 20:S42, 1988).

**Authors' abstract**

LAM applicants were studied to investigate the relationship between self-reported infectious episodes (IE), training data, and LAM participation. Eight days before the LAM, 4926 of 12,200 applicants were randomly selected, and sent a pilot-tested four page questionnaire 7 days after LAM. The 2311 respondents

were found to be 2.0 yr older and 7.6 min faster than the other LAM finishers ( $P < 0.01$ ). Univariate and multivariate analyses (logistic regression) were conducted to test the relationship between IE and km/wk of running (6 total categories). The final model tested controlled for age, marital status, reported sickness in other members of the runner's home, perceived feelings of stress in response to the personal training regimens, and the suppressive effect of sickness on regular training. In runners training  $\geq 97$  vs  $\leq 32$  km/wk, the odds ratio (OR) for IE during the 2 month period prior to the LAM was 2.0 (1.2-3.4) (95%CL), and a test for trends showed an increase in OR with increase in km/wk cat ( $P = 0.04$ ). Of the 1828 LAM participants sick-free before the LAM, 236 (12.9%) reported an IE during the week following the LAM vs 3 of 134 (2.2%) sick-free, similarly experienced runners who did not participate, OR = 5.9 (3.3-10.7). These data suggest that runners may experience increased odds for IE during heavy training or following a marathon race.

**250. Nieman, D.C. and**

**S.L. Nehlsen-Cannarella:**

The effects of acute and chronic exercise on immunoglobulins.

*Sports Medicine* 11:183-201, 1991.

**Authors' abstract**

The effects of acute exercise (both graded-maximal and submaximal) and exercise training on resting immunoglobulin levels and immunoglobulin production are reviewed. Brief graded-maximal or intensive short term submaximal exercise tends to be associated with increases in serum immunoglobulins, the pattern of which does not vary between athletes and nonathletes. Plasma volume changes appear to largely explain these acute increases. Acute moderate exercise, such as a 45-min bout of walking, on the other hand, has been associated with a transient rise in serum immunoglobulin levels despite no change in plasma volume. This increase is probably the result of contributions from extravascular protein pools and an increased lymph flow.

251. Nieman, D.C., S.L. Nehlsen-Cannarella, K.M. Donohue, D.B.W. Chritton, B.L. Haddock, R.W. Stout, and J.W. Lee: The effects of acute moderate exercise on leukocyte and lymphocyte subpopulations. *Medicine and Science in Sports and Exercise* 23:578-585, 1991.

**Authors' abstract**

The extent and duration of changes in circulating leukocyte and lymphocyte subpopulations, cortisol, and catecholamines were examined in 12 women who walked 45 min at 60%  $\dot{V}O_2$  max in a laboratory setting. A two factor, 2x6 design with repeated measures on both factors was utilized. The first factor was condition (exercise and rest), and the second factor was time (six points of measurement over a 24-h period), with treatment order counterbalanced. The 45-min walk, in comparison with rest in a seated position, was associated with a significant but moderate leukocytosis and lymphocytosis immediately following the walk. The leukocytosis was still evident after 3-h of recovery and was primarily due to a neutrophilia. The change in lymphocyte count, relative to baseline levels and the control condition, lasted less than 1.5 h, with an increase in the natural killer (CD16 and/or CD56) and cytotoxic T cell component (CD3 and CD16 and/or CD56) (NKCT) representing approximately two-thirds of the lymphocytosis and T cells (CD5) the other third. A significant decrease in the CD4:CD8 ratio was seen, with cytotoxic/suppressor (CD8) cells increasing and helper/inducer (CD4) cells demonstrating little change in comparison with baseline. This seems to have been due to a subpopulation of CD8 (low density antigen) cells, probably natural killer cells. The 45-min walk had no effect on plasma cortisol and epinephrine levels relative to the rest condition but was associated with a moderate increase in norepinephrine. In summary, compared with more intense forms of exercise in which plasma epinephrine levels rise, walking is associated with a much smaller increase in circulating numbers of total leukocytes and lymphocytes. In common with other modes of exercise except for marathon running, the lymphocytosis is represented primarily by NKCT and CD8 cells, resulting in a transient decrease in the CD4:CD8 ratio. However, the increase in CD8 cells is predominantly of the dimly fluorescent variety, suggesting that walking engenders a rise in natural killer cells with little change in other lymphocyte subpopulations.

252. Nieman, D.C., S.L. Nehlsen-Cannarella, P.A. Markoff, A.J. Balk-Lamberton, H. Yang, D.B.W. Chritton, J.W. Lee, and K. Arabatzis:

The effects of moderate exercise training on natural killer cells and acute upper respiratory tract infections.

*International Journal of Sports Medicine* 11:467-473, 1990.

**Authors' abstract**

A randomly controlled 15-wk exercise training (ET) study (five 45-min sessions/wk, brisk walking at 60% heart rate reserve) with a group of 36 mildly obese, sedentary women was conducted to investigate the relationship between improvement in cardiorespiratory fitness, changes in natural killer (NK) cell number and activity, and acute upper respiratory tract infection (URI) symptomatology. The study was conducted using a 2 (exercise and nonexercise groups)  $\times$  3 (baseline, 6-, and 15-wk testing sessions) factorial design, with data analyzed using repeated measures ANOVA. No significant change in NK cell number occurred as a result of ET as measured by the CD16 and Leu-19 monoclonal antibodies. ET did not have a significant effect on NK cell activity (E:T 50:1) especially during the initial 6-wk period ( $F(2,68) = 12.34$ ,  $P < 0.001$ ). Using data from daily logs kept by each subject, the exercise group was found to have significantly fewer URI symptom days/incident than the nonexercise group ( $3.6 \pm 0.7$  vs  $7.0 \pm 1.4$  days, respectively,  $P = 0.049$ ). Improvement in cardiorespiratory fitness was correlated significantly with a reduction in URI symptom days/incident ( $r = 0.37$ ,  $P = 0.025$ ) and a change in NK cell activity from baseline to six but not 15 weeks ( $r = 0.35$ ,  $P = 0.036$ ). In summary, moderate ET is associated with elevated NK cell activity after six but not 15 weeks, and reduced URI symptomatology in comparison to a randomized, sedentary control group.

253. Nieman, D.C., S.A. Tan, J.W. Lee, and

**L.S. Berk:**

Complement and immunoglobulin levels in athletes and sedentary controls.

*International Journal of Sports Medicine* 10:124-128, 1989.

**Authors' abstract**

Eleven marathon runners ( $42.7 \pm 2.1$  yrs.,  $54.2 \pm 1.8$  ml/kg/min) and nine sedentary controls ( $44.2 \pm 1.2$  yrs,  $33.3 \pm 1.1$  ml/kg/min) were studied during 30 min of rest, a graded maximal treadmill test using the Balke protocol,

and 45 min of recovery to determine the effects of training and acute exercise on complement and immunoglobulin levels. Three baseline and five recovery blood samples were obtained in addition to repeated 5-min samples during exercise. Data for the exercise period were analyzed using a multiple regression approach to repeated measures ANOVA to allow comparison between groups on a per cent  $\dot{V}O_2$  max basis. Groups did not differ during any of the three phases for IgG, IgA, or IgM. Resting levels of complement C3 ( $0.89 \pm 0.05$  vs  $1.27 \pm 0.10$  g/L,  $P < 0.001$ ) and C4 ( $0.19 \pm 0.02$  vs  $0.29 \pm 0.03$  g/L,  $P < 0.001$ ) were significantly lower in athletes than in controls. Exercise complement C3 ( $F, (1,18) = 14.1$ ,  $P = 0.001$ ) and C4 ( $F, (1,18) = 7.6$ ,  $P = 0.013$ ), and recovery complement ( $F, (1,18) = 19.4$ ,  $P < 0.001$ ) and C4 ( $F, (1,18) = 13.5$ ,  $P = 0.002$ ) were also lower in the athletes than in sedentary controls. Acute increases during exercise were not associated with changes in catecholamines or cortisol. These data suggest that blood concentrations of C3 and C4, but not IgG, IgA, or IgM, are decreased during rest, graded maximal exercise, and recovery in marathon runners in comparison with sedentary controls.

## 254. Northoff, H. and A. Berg:

Immunological mediators as parameters of the reaction to strenuous exercise.  
*International Journal of Sports Medicine* 12:S9-S15, 1991.

### Authors' abstract

Both the unspecific and the specific branch of the immune system are triggered and governed by contact and by a set of cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). These mediators, which are produced by activated macrophages and other cells, have also multiple (pleotropic) effects on different cells and organs. While TNF and IL-1 have strongly proinflammatory effects and seem to play a critical role in clinical situations such as septic shock, IL-6 has more restorative effects by being the main inducer of the acute phase response of the liver. The monokines also induce fever and release of ACTH in the brain. Strenuous exercise leads to a significant elevation of cytokines in the serum thereby eliciting an acute phase response. Analysis of systemic cytokines in the serum of marathon runners by the 7TD1 cell line assay revealed that the observed activity is very likely IL-6.

## 255. O'Connor, P.J. and D.L. Corrigan:

Influence of short-term cycling on salivary cortisol levels.

*Medicine and Science in Sports and Exercise* 19:224-228, 1987.

### Authors' abstract

The purpose of this study was to examine the response of salivary cortisol to acute exercise, and to directly compare serum and salivary cortisol responses to sub-maximal exercise. Eight males volunteered to participate in the study. On three separate days following the assessment of maximum oxygen uptake ( $\dot{V}O_{2\max}$ ), the subjects exercised on a bicycle ergometer at 75% of their  $\dot{V}O_{2\max}$  for 30 min. On a fourth day, the subjects rested quietly, and this served as a control condition. On each of these days, five serial samples of either blood, saliva, or both blood and saliva were obtained at 15-min intervals before, during, and after exercise. Sub-maximal exercise elicited a significant ( $P < 0.05$ ) increase in both serum and salivary cortisol above resting control levels immediately and 15 min following exercise under all exercise conditions. In addition, significant correlations (all  $P < 0.01$ ) were observed between serum and salivary cortisol at each of the five sampling periods. The correlations were as follows:  $r = 0.89$  at -15 min;  $r = 0.60$  at 0 min;  $r = 0.72$  at 15 min;  $r = 0.90$  at 30 min; and  $r = 0.93$  after 15 min of recovery. Saliva was also obtained immediately before and 5 min following the assessment of  $\dot{V}O_{2\max}$ , and there was a significant ( $P < 0.05$ ) increase in post  $\dot{V}O_{2\max}$  test ( $1.07 \pm 0.12$   $\mu\text{g}\cdot\text{dl}^{-1}$ ) compared to pre-test ( $0.71 \pm 0.06$   $\mu\text{g}\cdot\text{dl}^{-1}$ ) salivary cortisol levels. The results of this experiment indicate that salivary cortisol is a potentially valid measure of serum cortisol response to short-term cycling.

## 256. Ohira, Y., R.N. Girandola,

D.R. Simpson, and S. Ikawa:

Responses of leukocytes and other hematologic parameters to thermal dehydration.  
*Journal of Applied Physiology* 50:38-40, 1981.

### Authors' abstract

Effects of thermal dehydration without exercise on leukocyte differentials, serum protein fractions, and other hematologic characteristics were studied in six healthy subjects. Both leukocyte and serum total protein levels increased beyond that predicted by hemoconcentration alone. Eosinophil counts decreased significantly, although other leukocyte counts tended to increase. Serum globulin concentrations tended to increase, but the albumin level did not change. Serum  $\text{K}^+$  concentration was elevated, but  $\text{Na}^+$  and  $\text{Cl}^-$  were unaffected. It is suggested that thermal

dehydration affects blood leukocyte composition and protein metabolism in many of the same ways as physical exercise.

### 257. Oppenheimer, E.H. and R.A. Spaeth:

The relation between fatigue and the susceptibility of rats towards a toxin and an infection.

*American Journal of Hygiene* 2:51-66, 1922.

#### Synopsis

**Purpose** To determine whether fatigue will produce a greater susceptibility to toxins and infection in experimental animals.

#### Methods

1. White, hooded, healthy rats were run in an apparatus consisting of 2 sets of drums with three drums in each set. Each drum was mounted on a bicycle hub and was turned by an electric motor.
2. 22 rats were divided into 3 groups. The first group (control) was injected with tetanus toxin. The second group was fatigued before injection. The third group was fatigued both before and after injection.
3. 78 rats were injected with Type I pneumococcus and fatigued once before injection, or three times after injection.
4. 17 more rats were injected with pneumococcus: 6 were controls, 6 were fatigued before injection, and 5 were fatigued after injection.

#### Results

1. Fatigue before injection of pneumococci was nearly twice as potent in raising the resistance to this infection as was fatigue which follows injection.
2. The susceptibility of white and hooded rats to tetanus toxin was far greater than has hitherto been supposed. The M.L.D. was 0.00,000,004 gr. toxin per gram weight of rat.
3. Fatigue, induced artificially in white and hooded rats by forcing them to run in motor-driven drums, apparently tended to increase slightly their resistance to subcutaneous injections of tetanus toxin. This occurred whether fatigue precedes or follows the injection of the toxin.
4. White and hooded rats, up to 185 grams in weight, were not susceptible to diphtheria toxin in doses as large as 2 c.c.
5. Fatigue, both preceding and following intraperitoneal injection of Type I pneumococcus, definitely increased the resistance of the white and hooded rats to infection.

#### Conclusion.

1. At least in the case of white and hooded rats, our results contradict the popular belief that a fatigued individual is more susceptible to disease (tetanus toxin and pneumococcus infection) than a non-fatigued individual.

### 258. Order, U., H. Riedel, H. Liesen, W. Widenmayer, T. Hellwig, and

#### S. Geist:

Leukozyten und Lymphozytensubpopulationen.  
*Deutsche Zeitschrift für Sportmedizin* 40:22-29,  
1989.

#### Authors' abstract

In 33 male long-distance runners, leucocytes and lymphocyte subsets (CD3+, CD3+Leu-19+, CD3+CD25+, CD4+, CD4+Leu-8+, CD4+Leu-8-, CD8+, CD16+, CD19+) were measured by flow cytometry during an intensity-controlled preparatory training and after a 31-km race. Total lymphocytes and the subsets CD3+, CD4+, and CD4+Leu-8- were significantly reduced after 5 weeks of running training. One hour after the 31 km race exercise-induced individually highly differing lymphopenias and granulytosis could be found; monocytes also increased significantly;  $\bar{X} = 0.51$  lymph./15.2 gran./0.69 mono [ $10^9/l$ ]. As a result of an inappropriately high reduction of CD8+ to CD4+ cells, the ratio of T-helper/suppressor cells rose significantly. Three days after the race, a repeated decrease of all leucocytes (except granulocytes) and lymphocyte subsets (except B cells) was determined, whereas a significant increase of activated T-lymphocytes (which expressed interleukin-2 receptors at the same time) could be found one day and three days after the race. The results point out alterations of cell counts varying in time and partly in direction with an exercise-induced mobilization of granulocytes and monocytes as well as a delayed stimulation of the T cell repertoire. From endocrinological and neuroimmunological views, possible reasons are discussed in respect to increased susceptibility of athletes to infections.



**259. Oshida, Y., K. Yamanouchi,**

**S. Hayamizu, and Y. Sato:**

Effect of acute physical exercise on lymphocyte subpopulations in trained and untrained subjects. *International Journal of Sports Medicine* 9:137-140, 1988.

**Authors' abstract**

To clarify the difference in immunity between untrained subjects and well-trained athletes, the number of total leukocytes (WBC), lymphocytes, and neutrophils, percentages of various lymphocyte subpopulations (OKT3, OKT4, OKT8, Leu7, OKIa1), and the levels of lymphocyte transformation response to phytohemagglutinin (PHA) were determined in five untrained male subjects and six male athletes before, immediately after, and 24 and 72 h after acute physical exercise at 60% of  $\text{VO}_2$  max for 2 h. Exercise produced a significant rise in the number of WBC, lymphocytes, and neutrophils in both groups. Immediately after exercise, the percentage of OKT3 or OKT4 positive cells had significantly decreased in both groups, whereas that of OKT8 positive cells had markedly increased only in the athletes. Neither group showed any change in the percentage of OKIa1 positive cells. In both groups, the response of lymphocytes to PHA immediately after exercise was significantly lower than before, 24 h and 72 h after exercise. The level of Leu7 positive cells rose remarkably immediately after exercise in the athletes, but not significantly in the untrained subjects. These results suggest that an increase in Leu7 positive cells provides added host defense capacity in trained athletes during periods of stress which impair T-lymphocyte function.

**260. Österback, L. and Y. Qvarnberg:**

A prospective study of respiratory infections in 12-year-old children actively engaged in sports. *Acta Paediatrica Scandinavica* 76:944-949, 1987.

**Authors' abstract**

Data on the incidence of respiratory tract infections, antimicrobial treatment, days with fever and absence from school on account of these infections were studied in children participating in extracurricular sports activities with regular supervised training and competitive events. Swimmers, ice-hockey players and apparatus gymnasts were compared to a control group of children. Their mean age was 12.7 years at the end of the one year study. The children were examined three times during the year. More information was collected by a nurse who contacted the mothers of the children every two months. The girls had contracted more respiratory tract infections than the boys during the study. This difference was only seen regarding

common colds, not regarding major bacterial respiratory infections, i.e., otitis media, tonsillitis, sinusitis and pneumonia. Because of this difference the results were analyzed separately for the sexes. No differences between the sports and the control groups were seen in any respect regarding respiratory infections. Contrary to general opinion, sports participation does not seem to have a preventative effect on the occurrence of respiratory infections in children.

**261. Østerud, B., J.O. Olsen, and**

**L. Wilsøgaard:**

Effect of strenuous exercise on blood monocytes and their relation to coagulation. *Medicine and Science in Sports and Exercise* 21:374-378, 1989.

**Authors' abstract**

Changes were explored in the behavior of circulating monocytes and their potential association with the activation of the coagulation system as assessed following strenuous exercise. Twelve men and nine women from the Norwegian national cross country skiing team and 19 men and six women from a level just below that of the national team were studied before and after ski race competition. Mononuclear cells were isolated after incubation of heparinized blood with lipopolysaccharides (LPS;  $3 \text{ ng}\cdot\text{ml}^{-1}$ ) for 2 h. After a 50 km race for men, the specific thromboplastin activity of the stimulated monocytes rose from  $3.5 \times 10^{-3}/10^6$  cells to  $21.4 \times 10^{-3}/10^6$  cells. This probably reflects the mobilization of a new population of monocytes that are more sensitive to such stimuli. Resting top-athlete skiers had monocytes which were significantly less responsive to the LPS stimulus compared to nontrained people. There was an inverse correlation of plasma factor VII and the monocyte responsiveness to *in vitro* stimulation ( $r = 0.814$ ;  $P < 0.002$ ) from blood drawn after a race. Furthermore, factor VII was significantly reduced after a 50 km race, and a modest decline in the fibrinogen level was also observed ( $P < 0.05$ ). It is concluded that endurance ski racing causes white cell mobilization and more active white cells that may induce activation of the coagulation system and account for the involvement of factor VII and fibrinogen.

## 262. Oyster, N.:

Changes in plasma eosinophils and cortisol of women in competition.

*Medicine and Science in Sports and Exercise*

12:148-152, 1980.

### Author's abstract

This study investigated degrees of stress in ten advanced and high intermediate college women tennis players when competing against other women and when competing against men. Evidence of stress was determined through fluctuations in the plasma eosinophil and cortisol levels. Blood samples were drawn three times (prior to exercise, after a five minute warm-up and after 15 minutes of competition) on each of the four days of testing. Each sample was analyzed for eosinophil counts and cortisol. Changes in eosinophil counts of 30 percent or more were considered significant. There appeared to be a trend toward eosinopenia during competition as compared with warm-up. None of the chi-squares comparing competition against men with competition against women was significant. Cortisol changes were analyzed using ANOVA. Again none of the competitive cortisol differences was significant among male or female competitors. When the cortisol data was pooled, significant differences in response to stress were found between the individual players. Individual responses were examined separately in the text of this article.

## 263. Pahlavani, M.A., T.H. Cheung,

J.A. Chesky, and A. Richardson:

Influence of exercise on the immune function of rats of various ages.

*Journal of Applied Physiology* 64:1997-2001, 1988.

### Authors' abstract

The purpose of this study was to determine whether exercise could prevent the age-related decline in mitogenesis, which has been well documented in rats, mice and humans. At 1, 6, 12, and 18 mo of age, male Fischer F344 rats were subjected daily to swimming exercise for 6 mo. At the end of the 6-mo training period, spleen lymphocytes were isolated from the exercised rats and from age-matched sedentary controls. The induction of lymphocyte proliferation was measured with the mitogens concanavalin A (ConA) and lipopolysaccharide (LPS). In addition, the ability of the lymphocytes to produce interleukin 2 (IL2) in response to ConA induction was measured. ConA- and LPS-induced proliferation decreased 41-63% between 7 and 25 mo of age in both exercised and sedentary control rats. ConA-induced IL2 production decreased 42 and 62% between 7 and 25 mo of age for exercised and sedentary control rats,

respectively. Although the age-related decline in mitogen-induced proliferation and IL2 production was smaller in exercised rats, this was due to a lower level of mitogenesis and IL2 production in lymphocytes from young exercised rats. Exercise resulted in a significant decrease (23-32%) in mitogen-induced lymphocyte proliferation and IL2 production in 7-mo-old sedentary rats. However, in the 18- and 24- mo-old rats, mitogen-induced lymphocyte proliferation and IL2 production was not significantly different between exercised and sedentary control rats.

## 264. Papa, S., M. Vitale, G. Mazzotti, L.M. Neri, G. Monti, and F.A. Manzoli:

Impaired lymphocyte stimulation induced by long-term training.

*Immunology Letters* 22:29-33, 1989.

### Authors' abstract

In recent there has been increasing interest in the definition of hormone influence on the immune system. Physical stress provides a suitable model for studying the interactions between the immune system and the neuro-endocrine factors which have been shown to modulate the lymphoid cellular compartment. Our approach has been devoted to defining the stable modifications induced in the immune system in athletes during agonistic training. The results show that the circulating compartment of the immune system tends to modulate its different subsets under the continuous influence of stress hormones, together with a specific functional impairment of the helper subset in the proliferative response after stimulation with PHA, and particularly with PWM.

## 265. Papageorgiou, N., M. Carroll, S.R. Durham, T.H. Lee, G.M. Walsh, and A.B. Kay:

Complement receptor enhancement as evidence of neutrophil activation after exercise-induced asthma. *Lancet* 2:1220-1223, 1983.

### Authors' abstract

To determine whether neutrophils are activated after exercised-induced asthma, increases in neutrophil complement receptor numbers (complement receptor enhancement) were measured by the rosette technique. In twelve asthmatic patients there was a time-dependent rise in complement receptor numbers for up to 60 min after treadmill exercise. This enhancement of complement receptors was preceded by a rise in plasma neutrophil chemotactic activity and a reduction in the peak expiratory flow rate. These changes could be inhibited by prior

administration of disodium cromoglycate. The changes were not observed in seven asthmatic patients in whom asthma was not induced by an identical exercise task. Complement receptor enhancement was also observed *in vitro* when partially purified neutrophil chemotactic activity from a patient with exercise-induced asthma was incubated with normal neutrophils. These findings suggest that inflammatory cells are activated after exercise-induced asthma, possibly as a result of the release of neutrophil chemotactic activity and other mast-cell associated mediators.

**266. Parry-Billings, M., E. Blomstrand, N. McAndrew, and E.A. Newsholme:**

A communicational link between skeletal muscle, brain, and cells of the immune system.  
*International Journal of Sports Medicine*  
11:S122-S128, 1990.

**Authors' abstract**

The present paper reviews evidence for the role of specific amino acids in the etiology of fatigue and the overtraining syndrome in athletes. An increase in the plasma concentration ratio of free tryptophan: or branched-chain amino acids may mediate an increase in %-HTT synthesis in the brain and thus induce fatigue during exercise. Glutamine is essential for the proper functioning of cells of the immune system and a decrease in plasma glutamine concentration post-exercise and in overtraining may induce an impairment in immune function. Branched-chain amino acids may play a central role in both these processes. Thus, they compete with free tryptophan for entry into the brain. Branched-chain amino acids may also be important in skeletal muscle or important in the control of glutamine release from muscle. Consequently, the metabolism of glutamine, tryptophan, and branched-chain amino acids may be the key to understanding some aspects of central fatigue and some aspects of immunosuppression that are very relevant to athletic endeavor. They may be also relevant to other physiological and pathological conditions.

**267. Pedersen, B.K.:**

Influence of physical activity on the cellular immune system: Mechanisms of action.  
*International Journal of Sports Medicine*  
12:S23-S29, 1991.

**Author's abstract**

This review deals with the effect of acute physical exercise and training status on different components of the immune system. Predominantly studies in humans are

mentioned. In relation to acute physical exercise (75% of  $\text{VO}_2\text{max}$ , 1 hour) the leukocyte concentration increased; following exercise the neutrophils increased fourfold. The lymphocyte concentration increased during and decreased following exercise. The percentage of CD3+ cells (pan T cells) declined during exercise, mainly due to a fall in the %CD4+ cells. The %CD16+ cells (NK cells) increased twofold and returned to prevalue two hours after exercise. The %CD20+ cells (B cells) did not change in relation to exercise, whereas the %CD14+ cells (monocytes) increased two to threefold following exercise. The NK cell activity increased during but decreased following exercise. These increases were due to recruitment of NK cells with a high IL-2 response capacity, whereas the decreased NK activity post-exercise was due to down-regulation by prostaglandins released by the elevated concentration of monocytes. During severe, moderate, as well as light exercise, the NK cell activity increased, but the post-exercise suppression of the NK cell function was found only following severe exercise, and not after moderate or light exercise; furthermore, only following severe exercise, an increased monocyte concentration was demonstrated. The IL-2-stimulated lymphocyte proliferative response increased due to stimulation of CD16+ cells and did not reflect expression of IL-2 receptors. Following exercise, increased production of interleukin 1 (IL-1) and interleukin 6 (IL-6) were found, whereas we were unable to show any exercise-induced changes in the production of the tumor necrosis factor (TNF), interleukin 2 (IL-2) or interferon- $\gamma$  (IFN- $\gamma$ ). Using a reverse plaque forming cell (PFC) assay, it was shown that exercise induced significantly decreased numbers of IgG-, IgA- and IgM-secreting blood mononuclear cells. Purified B cells produced plaques only after EBV stimulation and in these cultures no exercise-induced suppression was found. The suppression of the PFC response was shown to be mediated by monocytes. The NK cell activity and the production of IL-1 have been shown to be elevated in trained versus untrained, whereas the concentration of secretory IgA was lower in the trained. In this review, the possible role of different stress hormones is discussed. Results are presented showing that selective administration of epinephrine to obtain plasma concentrations identical with those seen during exercise mimicked the exercise-induced effects of NK activity, lymphocyte proliferative response and blood mononuclear cell subsets, but not totally the effect on neutrophils. It is concluded that exercise-induced immunomodulation occurs due to altered composition of immunocompetent cells as well as due to activation of the immune system; furthermore, that during severe as well as moderate exercise, the immune system is enhanced, whereas severe exercise only causes post-exercise immunodepression.

**268. Pedersen, B.K., N. Tvede,**

**L.D. Christensen, K. Klarlund,**

**S. Kragbak, and J. Halkjaer-Kristensen:**

Natural killer cell activity in peripheral blood of highly trained and untrained persons.

*International Journal of Sports Medicine*  
10:129-131, 1989.

**Authors' abstract**

Natural killer (NK) cell activity and concentration of CD16+ cells (NK cells) and CD20+ cells (monocytes) in peripheral blood were measured in highly trained racing cyclists and in age- and sex-matched untrained controls. Median NK cell activity was 38.1% (range 20.0%-57.1%) in trained vs 30.3% (range 19.7%-43.1%) in untrained (P = 0.008). Median %CD16+ cells was 17% (range 7%-33%) in trained vs 11% (3%-29%) in untrained (P = 0.007). Indomethacin *in vitro* enhanced the NK cell activity in both groups. There was, however, no significant difference between the NK cell activity in trained and untrained after exposure to indomethacin *in vitro*. Indomethacin-enhanced NK cell activity was 45.9% (range 24.4%-67.5%) in trained and 40.0% (range 23.9%-68.5%) in untrained (P = 0.138). Mean % CD14+ cells was 8.3% (range 2%-15%) in trained vs 3.8% (2%-8%) in untrained (P < 0.0001). The increased NK cell function thus demonstrated in highly trained persons might result in better resistance against infectious disease.

**269. Pedersen, B.K., N. Tvede, F.R. Hansen,**

**V. Andersen, T. Bendix, G. Bendixen,**

**K. Bendtzen, H. Galbo, P.M. Haahr,**

**K. Klarlund, J. Sylvest, B.S. Thomsen,**

**and J. Halkjaer-Kristensen:**

Modulation of natural killer cell activity in peripheral blood by physical exercise.

*Scandinavian Journal of Immunology* 27:673-678, 1988.

**Authors' abstract**

The present study was designed to examine the effect of physical exercise on human natural killer (NK) cells. Six healthy volunteers underwent two different acute physical exercise tests with an interval of at least 1 week: (1) 60 min bicycle exercise at 80% of maximal oxygen uptake ( $\dot{V}O_2$  max) and (2) 60 min back-muscle training at up to 29% of  $\dot{V}O_2$  max; blood samples were collected before and during the last few minutes of exercise, as well as 2 h and 24 h afterwards. The NK cell activity (lysis/fixed number of mononuclear cells) increased during bicycle exercise, dropped to a minimum 2 h later

and returned to pre-exercise levels within 24h. Back muscle exercise did not significantly influence NK cell activity. Plasma levels of adrenaline, noradrenaline, and cortisol were elevated during bicycling, but not during back-muscle exercise, indicating that exercise intensity is a determinant of NK cell activity. During bicycle exercise the NK cell subset (CD16+ cells) of mononuclear cells increased significantly. Furthermore an improved interleukin 2 (IL-2) boosting of the NK cell activity was found during work as compared to IFN- $\alpha$  and indomethacin-enhanced NK cell activity. These results indicate that NK cells with a high IL-2 response capacity are recruited to the peripheral blood during exercise. The decreased NK cell activity demonstrated 2 h after work was probably not due to fluctuations in size of the NK cell pool, since the proportion of CD16+ cells was normal. The finding that indomethacin fully restored the suppressed NK cell activity *in vitro* and the demonstration of a twofold increase in monocyte (CD20+ cells) proportions 2 h after work, strongly indicate that prostaglandins released by monocytes during the heavy physical exercise are responsible for the down-regulation of the NK cells.

**270. Pedersen, B.K., N. Tvede, K. Klarlund,**

**L.D. Christensen, F.R. Hansen, H. Galbo,**

**A. Kharazmi, and J. Halkjaer-Kristensen:**

Indomethacin *in vitro* and *in vivo* abolishes post-exercise suppression of natural killer cell activity in peripheral blood.

*International Journal of Sports Medicine*

11:127-131, 1990.

**Authors' abstract**

The present study was designed to explain the mechanism of the post-exercise down-regulation of human natural killer (NK) cell activity recently described by us. Fifteen young, healthy volunteers underwent 60 min of bicycle exercise at 75% of maximal oxygen uptake ( $\dot{V}O_2$  max). Six of the volunteers were exercised twice with an interval of at least one month. At the second exercise test they received oral indomethacin. Blood samples were collected before and during the last minutes of exercise as well as 2 h and 24 h after work. The NK cell activity (lysis fixed number of mononuclear cells) increased during bicycle exercise, dropped to a minimum 2 h later and returned to pre-exercise levels within 24 h. During bicycle exercise the percentage of NK cells (CD16+ cells) of mononuclear cells increased significantly but returned to normal within 2 h after exercise. Two hours after exercise, however, increased monocyte cell count and neutrophils were found. The *in vitro* release of prostaglandin E2 from mononuclear cells was increased. Furthermore, the neutrophil chemiluminescence response

was also increased in the 2 h post-exercise period; this response is associated with prostaglandin E2 production by neutrophils. Indomethacin, whether administered in vivo or in vitro, fully restored the suppressed post-exercise NK cell activity. Finally, the NK cell activity of monocyte depleted mononuclear cells did not decrease below basal levels after exercise. These findings strongly indicate that prostaglandins released from monocytes and neutrophils are involved in the post-exercise down-regulation of NK cells.

#### **271. Pershin, B.B., B.A. Emelyanov,**

**Ya.A. Sokolov, and S.N. Kuzmin:**

Study of the mechanism of the phenomenon of immunoglobulin disappearance in a stress environment. (In Russian).

*Patologicheskaya Fiziologiya i Eksperimentalnaya Terapiya* 5:41-44, 1987.

#### **Authors' abstract**

Animal experiments showed that during intensive physical exertion (swimming) considerable absorption of injected radioactive label ( $^{125}\text{I}$ -IgG) by the formed elements of the blood and its excretion into the environment (water) occur. Intensive physical exertion is attended by sharp reduction of the mean levels of serum immunoglobulins; in individual analysis complete disappearance of immunoglobulins of some classes was registered in some of the animals. Comparison of the results provides evidence of the sorption mechanism of the disappearance of immunoglobulins from circulation in their increased secretion into the environment.

#### **272. Peters, E.M. and E.D. Bateman:**

Ultramarathon running and upper respiratory tract infections.

*South African Medical Journal* 64:582-584, 1983.

#### **Authors' abstract**

Opinions differ as to whether marathon runners have an increased susceptibility to upper respiratory tract (URT) infections after a race. In an attempt to answer this question, we carried out a prospective study of the incidence of symptoms of URT infections in 150 randomly selected runners who took part in the 1982 Two Oceans Marathon in Cape Town, and compared this with the incidence in individually matched controls who did not run. Runners were questioned on the day before and 2 weeks after the race. Symptoms of URT occurred in 33.3% of runners compared with 15.3% of controls, and were most common in those who had achieved the faster race times. The incidence in slow runners was no greater than that in

controls. Fast runners also experienced more musculoskeletal pain during and after the race. These results suggest a relationship between acute stress and susceptibility to URT infections. Impairment of one or more local mucosal or general host defences may account for this effect.

#### **273. Petrova, I.V., S.N. Kuz'min,**

**T.S. Kurshakova, R.S. Suzdal'nitskiy,**

**B.B. Pershin, Ye.B. Kovalenko,**

**V.A. Levando, and I.Ya. Moshiaishvili:**

Phagocytic activity of neutrophils and humoral factors of systemic and local immunity during intensive physical loads. (In Russian).

*Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* 12:53-57, 1983.

#### **Synopsis**

**Purpose** To study the phagocytic activity of neutrophils and to determine the levels of normal serum and secretory antibodies and immunoglobulins in athletes as physical loads were increased in time and intensity.

#### **Methods**

1. 91 athletes between ages 19 to 21 were examined.
2. Three groups (30 people each) engaged in three different training programs of increasing volume and intensity, the fourth group (control) engaged in no physical or emotional loads.

3. Phagocytic activity of neutrophils in peripheral blood was determined using heat killed strains of intestinal bacillus and *Staphylococcus aureus*.

#### **Results**

1. An increase in exercise load (II and III groups) led to a reliable reduction in phagocytosis.
2. As the load time and intensity were raised, the number of immunologic indices that were decreased, compared with the control group values, became larger.

#### **Conclusions**

1. Differences were detected in phagocytic activity of neutrophils with respect to intestinal bacillus and staphylococcus in persons not involved in athletics and in athletes during various physical loads.
2. The oppositely directed trend toward change in the indices of phagocytic activity of neutrophils observed during light physical loads is replaced by their reliable reduction compared with control group indices, when the physical loads were heavier.

3. The reduction in functional activity of the neutrophils in response to increasing physical loads coincides with a reduction in the content of normal antibodies, immunoglobulins and lysozyme.

- 274. Pincemail, J., G. Camus, A. Roesgen, E. Dreezen, Y. Bertrand, M. Lismonde, G. Deby-Dupont, and C. Deby:**  
Exercise induces pentane production and neutrophil activation in humans. Effect of propranolol.  
*European Journal of Applied Physiology* **61**:319-322, 1990.

#### Authors' abstract

The effect of  $\beta$ -adrenergic receptor blockade on exercise-induced lipid peroxidation in man has been examined by measuring the production of pentane in expired air. For this purpose, five healthy male subjects were subjected to dynamic exercise of graded intensity on a cycle ergometer (10 min at 45%, 5 min at 60% and 75% maximal oxygen uptake 1 h after ingestion of either a placebo or 40-mg propranolol). At rest, mean pentane concentration (ppent) with placebo was  $4.13 \text{ pmol} \cdot \text{l}^{-1}$ , SD 2.14. After exercise, this value significantly increased by 310% ( $17.1 \text{ pmol} \cdot \text{l}^{-1}$ , SD 7.73,  $P < 0.01$ ). Oral administration of 40-mg propranolol significantly lowered the mean resting [pent] to  $1.75 \text{ pmol} \cdot \text{l}^{-1}$ , SD 0.77,  $P < 0.05$ . After exercise, the increase of [pent] was much smaller (240%) and was less significant ( $P < 0.2$ ) than with the placebo. The mechanism of this inhibitory effect of propranolol remains to be elucidated. However, as indicated by the measurement of plasma myeloperoxidase concentration it can be concluded that the antioxidant property of propranolol cannot be attributed to the inhibition of neutrophil activation, a possible source of free radicals during exercise.

- 275. Reinherz, E.L. and S.F. Schlossman:**  
Regulation of the immune response-inducer and suppressor T-lymphocyte subsets in human beings.  
*New England Journal of Medicine* **303**:370-373, 1980.

#### Authors' abstract

Immune homeostasis results from a delicate balance of inducer and suppressor subsets within the human T-cell circuit. Perturbations in subset dynamics may initiate a variety of immunopathologic disorders. For example, immunodeficiency may result from either a loss of the inducer T-cell subset or activation of the suppressor cell population. Alternatively, autoimmunity may follow unopposed activation of the inducer population or loss of

suppressor-cell influence. An understanding of this circuit will be important for the elucidation of the pathogenesis of a number of diseases and should permit the orderly manipulation of the human immune response through modulation of selected T-cell subsets.

- 276. Repsher, L.H. and R.K. Freebern:**  
Effects of early and vigorous exercise on recovery from infectious hepatitis.  
*New England Journal of Medicine* **281**:1393-1396, 1969.

#### Authors' abstract

To compare the effect of strenuous exercise on recovery time in 199 American servicemen in Vietnam with infectious hepatitis to that in 199 patients with infectious hepatitis treated in the customary fashion, the exercise group was started on the program of strenuous exercise for approximately three hours daily at the time their symptoms were considered to be slight, irrespective of the degree of liver-function abnormality. No statistical difference was found between the two groups in the duration of elevation of serum bilirubin or in relapse rate. Exercise did not adversely affect those whose maximum serum bilirubin was greater than  $3.0 \text{ mg per } 100 \text{ ml}$  or those over 30 years old. No difference in duration of disease was found in those who were involved in strenuous activity at the time of onset of illness as compared to those involved in light activity. Strenuous activity does not appear to have any adverse effect on the acute course of infectious hepatitis in previously healthy young men.

- 277. Reyes, M.P. and A.M. Lerner:**  
Interferon and neutralizing antibody in sera of exercised mice with coxsackievirus B-3 myocarditis.  
*Proceedings of the Society for Experimental Biology and Medicine* **151**:333-338, 1976.

#### Authors' abstract

ICR Albino Swiss mice were inoculated i.p. with  $1.9 \times 10^4$  PFU of coxsackievirus B-3 (Nancy) and subsequently forced to swim vigorously daily in a preheated pool. Viremias and virus in hearts of exercised mice were, respectively,  $75 \times$  to  $1000 \times$  greater than in infected, but not exercised mice. At 24 hr after inoculation, pooled serum from mice that had been swum had no circulating interferon, while infected but not swum mice had interferon activity at a dilution of 1:10. At 72 hr after infection, circulating interferon disappeared from infected (not swum) mice, but continued to be present in high titres through the sixth day in sucklings forced to swim.

Interferon was first detected in the hearts of both groups at 48 hr. Quantities in both infected groups were generally similar. Neutralizing antibodies were found in these baby mice on the 13th day of infection and were  $16 \times$  greater in nurslings that were not exercised. Measures of corticosterone taken at 4 pm daily were similar in infected, infected-swum, and uninfected mice. The present experiments confirm that after i.p. inoculation with the Nancy strain of coxsackievirus B-3, swimming nursing albino Swiss ICR mice results in a remarkable increase in virus multiplication in the hearts. When compared with infected, but not swum controls, an increase in magnitude of viremia also results.

**278. Reyes, M.P., A.M. Lerner, and K-L. Ho:**

Diminution in the size of the thymus in mice during forced swimming.

*Journal of Infectious Diseases* 143:292, 1981.

**Authors' abstract**

When compared with rested animals on days 3 and 6 (experiment 1) and days 6 and 9 (experiment 2) during forced swimming, significant decreases in mean thymic index in the exercised mice were evident. Thymuses from exercised animals were small and their cortex was thinned, but the density and appearance of the retained thymocytes appeared normal. There was no obvious necrosis of the thymocytes. At 96 hr after cessation of forced swimming, thymic indices were similar, and normal thymic configuration returned. No discernible changes occurred in gross or histologic appearance of the spleen or in splenic indices. In 1956 Selye reported that rats forced to exercise severely on a treadmill developed atrophic thymuses, lymph nodes, and spleens. The data given in the present study do not define the mechanism for change in the size of the thymus and lack of change in the spleen during forced swimming. The change could be from stress-induced release of corticosteroids causing thymocyte lysis. Other mechanisms, such as altered T-cell circulation induced by exercise, are possible.

**279. Reyes, M.P., J.A. Thomas, K-L. Ho, F.E. Smith, and A.M. Lerner:**

Elevated thymocyte norepinephrine and cyclic guanosine 3',5' monophosphate in T-lymphocytes from exercised mice with coxsackievirus B3 myocarditis.

*Biomedical and Biophysical Research Communications* 109:704-708, 1982.

**Authors' abstract**

On the ninth day after coxsackievirus B3 infection in adolescent ICR Swiss mice, norepinephrine levels in the thymus in infected-swum mice (Group III) were significantly greater than those in infected (Group II) but not exercised controls. Similarly, levels of thymocyte cyclic 3',5' guanosine monophosphate were elevated. After isoproterenol, thymocytes from exercised, healthy, uninfected mice (Group IV) generated enhanced levels of cyclic 3',5' adenosine monophosphate, but beta stimulated thymocytes from mice in Group III failed to raise levels of cyclic 3',5' adenosine monophosphate. Rises in T-lymphocyte norepinephrine and cyclic 3',5' guanosine monophosphate accompany a concomitant decrease in cyclic 3',5' adenosine monophosphate in CB3-infected and swum mice.

**280. Richter, E.A., B. Kiens, A. Raben, N. Tvede, and B.K. Pedersen:**

Immune parameters in male athletes after a lacto-ovo vegetarian diet and a mixed Western diet.

*Medicine and Science in Sports and Exercise* 23:517-521, 1991.

**Authors' abstract**

The influence of a lacto-ovo vegetarian diet versus a meat-rich Western diet on *in vitro* measures of immune function was studied in eight male endurance athletes. Subjects consumed two different diets for  $2 \times 6$  wk, separated by 4 wk on an *ad libitum* diet, in a cross-over design. Both diets consisted of 57 energy % (E%) carbohydrates, 14 E% protein and 29 E% fat. One diet was a mixed meat-rich diet (M) prepared with 69% animal protein sources, whereas the other diet (V) was a lacto-ovo vegetarian diet prepared with 82% vegetable protein sources. Blood for determination of leukocyte subpopulations and *in vitro* function was collected at the end of each diet period 36 h after the last training bout. Fiber content and P/S ratio of fatty acids were twice as high on the V diet as on the M diet. Training volume was similar on the two diets, and maximal aerobic capacity did not change during diet periods. The number of CD3<sup>+</sup> (pan T-cells), CD8<sup>+</sup> (mainly T suppressor cells), CD4<sup>+</sup>

(monocytes) was similar after the two different diets. Similarly, proliferations of mononuclear cells after stimulation with interleukin-2 (IL-2), phytohemagglutinin, and purified derivative of tuberculin (PPD), as well as activity of natural killer cells in the unstimulated state and after stimulation with IL-2, indomethacin, and interferon-alpha (IFN-alpha), were identical after the two diet periods. It is concluded that, in male athletes, the concentration, composition, and *in vitro* function of human blood mononuclear cells are unaffected by whether the diet in the preceding 6 wk has been a meat-rich mixed diet or a lacto-ovo vegetarian diet.

### 281. Ricken, K.-H. and W. Kindermann:

Der immunstatus des Leistungssportlers - Ursachen der Infektanfälligkeit.  
*Deutsche Zeitschrift für Sportmedizin* 37:38-42, 1986.

#### Authors' abstract

After a short introduction to immunology the causes of susceptibility to infections are explained. Our own examinations of 153 athletes refer to the following parameters: lysozyme, PMN elastase, the complement factors C3 and C4, total protein fraction, electrophoresis, the immunoglobulins IgG, IgM, IgA, and IgD,  $\alpha_2$ -macroglobulin, haptoglobin,  $\alpha_1$  acid-glycoprotein, the minerals magnesium and calcium, the trace elements zinc and copper and the percentage of T- and B-lymphocytes and natural killer cells. A deficiency of lysozyme in 48%, of zinc in 78.8%, of magnesium in 70.3% and of T-lymphocytes in 82% was striking. The increase of  $\alpha_2$ -macroglobulin in 70% correlated with the deficiency of zinc. The importance of the cellular immunity in the defense of infectious diseases and the necessity of an exact determination of the immunological status of athletes are emphasized.

### 282. Ricken, K.-H. and W. Kindermann:

Behandlungsmöglichkeiten der Infektanfälligkeit des Leistungssportlers.  
*Deutsche Zeitschrift für Sportmedizin*  
37:146-150, 1986.

#### Authors' abstract

The possibilities of treatment of the susceptibility to infections are explained, also in consideration of the naturopathy. Inosiplex, lyophilized bacterial lysate and preparations of immunoglobulins may be applied in sports medicine. Treatments corresponding to nature are phytotherapy, cell therapy and combined biological pharmacotherapy. A deficiency of the trace element zinc

and the minerals of magnesium and calcium should be balanced.

### 283. Ricken, K.-H. and W. Kindermann:

Cell-mediated immunity of male and female athletes.  
*International Journal of Sports Medicine* 8:157, 1987.

#### Authors' abstract

T-, B- and O-lymphocytes play an important role in the defense of infections and cancerous diseases. The percentages of lymphocytes was measured by monoclonal antibodies in 44 male and 22 female athletes in comparison to 20 non-athletes of both sexes. Whereas in male athletes there was a statistically significant difference in T- and O-lymphocytes compared to female athletes, a sex-linked difference was only evident in the O-lymphocytes of the leisure-time sportsmen. Significant sex-linked differences of T-, B- and O-lymphocytes were determined in the non-athletes. A significant decrease of the T-lymphocytes and increase of O-lymphocytes were measured in female as well as in male athletes compared to unconditioned individuals. The normal values of lymphocytes in the literature are varying very much and are not differentiated by sex. Therefore it is recommendable to evaluate findings of the cellular immunity of athletes in consideration of sex. It is impossible to interpret our findings on the basis of today's level of knowledge. We suggest to pay more attention to the cell-mediated immune function of athletes in the future.

### 284. Ricken, K.-H., T. Rieder, G. Hauck, and W. Kindermann:

Changes in lymphocyte subpopulations after prolonged exercise.  
*International Journal of Sports Medicine*  
11:132-135, 1990.

#### Authors' abstract

In order to assess the changes in the cellular immune system, 27 healthy male subjects were selected who participate in leisure-time sports and in whom measurement of the lymphocyte subsets in venous blood was carried out before and after a standardized endurance exercise test (E I, 60 minutes in length, intensity: 63% of maximum performance). The percentages of the following parameters were measured: total T-lymphocytes, B-lymphocytes and O-lymphocytes as well as T-4 lymphocytes (helper T-lymphocytes, CD4<sup>+</sup>) and T-8 lymphocytes (cytotoxic/suppressor T-lymphocytes, CD8<sup>+</sup>). In a subgroup consisting of 8 subjects, the



parameters indicated above were measured again 24 hours following E. In order to check the reproducibility of the findings, the endurance exercise test was repeated 2 1/2 weeks later (E II). At the end of E, the T-lymphocytes had decreased significantly in comparison to the initial value, whereas O-lymphocytes increased by the same amount. In addition, helper T-lymphocytes were decreased, and cytotoxic/suppressor cells were increased significantly. All changes had been reversed 24 hours following E. Between E I and E II there was no difference with respect to the changes in lymphocytes and their subpopulations. The data suggest that acute prolonged exercise influences the cellular immune system. The question as to the degree to which these immunological changes can be equated with a suppression of the cellular immune system and cause an enhanced susceptibility to infections in high-performance athletes cannot be conclusively answered on the basis of the present data.

**285. Rigsby, L., P. Raven, R. Dishman, and A. Jackson:**

The effects of exercise on HIV<sup>+</sup> individuals.  
*Medicine and Science in Sports and Exercise*  
21:S109, 1989.

**Authors' abstract**

The purpose of the study was to examine the effects of regular exercise training on fitness level, immunological response and depression in documented HIV<sup>+</sup> subjects. The sample included 38 males with an age range of 27 to 48. The subjects were clinically evaluated for their health status by a physician using a modified Walter Reed scale. The subjects were placed in two equally matched groups based upon the scale scores. The groups were then randomly assigned to exercise (E) or counseling (C) conditions. All subjects were pretested and posttested for fitness level, total white, lymphocyte, T4 and T8 blood cell counts and depression using the Beck Scale (BS). The fitness tests included a submaximal YMCA cycling test for which heart rate (HR) was recorded at 150 watts and a battery of strength tests. O<sub>2</sub> intake was not assessed due to potential transmission of infection. The subjects participated in a 12 week program of E or C. The E program consisted of 3 1-hour training sessions/week. Each training session consisted of flexibility, strength and endurance activities. The endurance activity was 25 minutes of stationary cycling following ACSM guidelines. The C condition included a 2-hour group counseling session/week led by a certified counselor. Data analysis indicated reductions in HR ( $m = 161 \pm 13.4$  to  $m = 142 \pm 9.9$ ,  $P < 0.01$ ) after training in the E group with no change in the C group. Strength changes followed this pattern. Blood cell count values did not change in

either group. BS scores were reduced across both groups ( $m = 8.5 \pm 8.0$  to  $4.4 \pm 4.9$ ,  $P < 0.05$ ). Thus, regular exercise will improve fitness and reduce absolute depression without negative effects on immunological response in HIV<sup>+</sup> individuals.

**286. Ringertz, O. and B. Zetterberg:**

Serum hepatitis among Swedish track finders. An epidemiologic study.  
*New England Journal of Medicine* 276:540-546, 1967.

**Authors' abstract**

During 1957-1963, 568 cases of serum hepatitis occurred among cross-country track finders in Sweden, showing an increasing number of cases each year. The diseases started in the western parts of Sweden and spread slowly over the whole country. The incubation period of the disease has been estimated to be ninety to one hundred and fifty days. Over 95% of the track finders were found to have received scratches or wounds during the competitions. The transmission of the disease is believed to have occurred through the inoculation of virus into these lesions mainly at the washings after the competitions. The epidemic was brought to an end when, among other regulations, adequate clothing was made compulsory. In 1965-1966 another outbreak, including 42 cases, occurred shortly after these regulations had been abolished. Since this manuscript was completed, a new outbreak of track-finders hepatitis has occurred. In December, 1963, a case was reported from Stockholm (District ) and in April, 1964, another from Smaland (C). No further cases occurred until April, 1965, when there was one case in northern Sweden (Y). During the summer and autumn of 1965, the number of cases increased rapidly, showing a peak during the winter months. In all, 41 cases were reported during the period July, 1965, to April, 1966. An investigation soon revealed that the Orienteering Associations at the start of the spring season in 1965 had abolished the regulations concerning the clothing at the competitions as well as the other regulations introduced during 1962. The regulations were reintroduced before the start of the spring season in 1966. During 1965-1966 most of the cases occurred in the western part of Sweden (districts E,F,G and H), in the Stockholm area (Q), in Dalarna (N) and in the far north of the country (X and Y). The distribution according to the competition classes was similar to that of 1961-1962. The incubation period was in all cases found to be ninety to one hundred and fifty days.

**287. Roberts, J.A.:**

Viral illnesses and sports performance.

*Sports Medicine* 3:296-303, 1986.

**Author's summary**

Recent evidence has shown that people undergoing severe mental or physical stress may have reduced immunity to viral infections. There are risks associated with strenuous physical activity during the acute phase of viral infection, and there are reports of sudden death and serious complications occurring in previously fit young adults who undertake vigorous exercise when in the acute phase of a viral illness. Abnormalities of skeletal muscle have been demonstrated in patients with viral infection and this may explain the loss of performance experienced by athletes after upper respiratory tract infection. As a general rule, for all but mild common colds, it is advised that the athlete avoids hard training for the first month after infection.

**288. Robertson, A.J., R.C. Potts,**

**M.C.K. Browning, J.H. Gibbs,**

**K. Ramesar, R.A. Brown, and J. S. Beck:**

The effect of strenuous exercise on plasma cortisol levels and circulating lymphocytes.

*Scottish Medical Journal* 24:255, 1979.

**Authors' abstract**

Healthy volunteers were exercised to exhaustion on a bicycle ergometer. The numbers of lymphocytes in venous blood forming E-rosettes or responding to PHA stimulation were measured precisely, before and at intervals after exercise (1 and 2). Immediately after exercise, all subjects showed a marked lymphocytosis: SIg cells rose by 5 to 15 percent and E-rosettes and PHA-responding cells showed a comparable fall. Fifteen minutes later, lymphocyte findings had returned virtually to pre-exercise levels. By contrast, plasma cortisol levels were relatively unchanged immediately after exercise but became markedly raised 15 minutes later: consequently, raised plasma cortisol levels cannot have caused the exercise-induced lymphocytosis but may have limited the duration of the lymphocytosis.

**289. Robertson, A.J., K.C. Ramesar,**

**R.C. Potts, J.H. Gibbs, M.C.K. Browning,**

**R.A. Brown, P.C. Hayes, and J.S. Beck:**

The effect of strenuous physical exercise on circulating blood lymphocytes and serum cortisol levels.

*Journal of Clinical and Laboratory Immunology* 5:53-57, 1981.

**Authors' abstract**

Venous blood was removed from healthy subjects immediately before and at intervals after exercise on a bicycle ergometer. Immediately after exercise, the subjects developed a lymphocytosis in which (a) the E-rosette percentage fell by 10% but their absolute number in the circulating blood rose by more than 70%, (b) the percentage of PHA-stimulated cells fell, but their absolute numbers increased considerably and (c) the absolute numbers of Con-A and PWM-responding cells increased. The numbers of lymphocytes in the various subpopulations had returned virtually to the pre-exercise levels 15 minutes after stopping exercise. During the response to exercise, the characteristics of the cells in the various subpopulations did not show any major changes, despite considerable and rapid fluctuations in numbers: it is suggested that exercise discharges intravascularly sequestered cells and that cortisol may be involved in re-sequestration of stress-released cells. It is recommended that, in clinical studies on circulating lymphocyte numbers and populations, the patient should be rested for at least 15 minutes before venesection.

**290. Röcker, L., K.A. Kirsch, and H. Stoboy:**

Plasma volume, albumin, and globulin concentrations and their intravascular masses. A comparative study in endurance athletes and sedentary subjects.

*European Journal of Applied Physiology* 36:57-64, 1976.

**Authors' abstract**

Plasma volume, hematocrit, intravascular protein concentration, colloid osmotic pressure and the intravascular mass of proteins were measured in 49 sedentary subjects and 40 endurance athletes (long-, middle distance runners, cyclists). The plasma volume in sedentary subjects was 42.7 (35.8-51.7) ml/kg body weight (BW) as compared to 54.6 (46.7-65.9) ml/kg BW in athletes. The protein concentrations were 71.0 (66.5-77.1) g/l in sedentary subjects and 69.0 (64.8-75.2) g/l in athletes. The respective numbers for the hematocrit were 44.6 (40.1-49.25) % and 42.8 (38.2-49.6) %, for the colloid osmotic pressure 38.0 (36.0-40.5) cm H<sub>2</sub>O

(n = 35) and 30.0 (25.0-34.4 ) cm H<sub>2</sub>O (n = 31), for the intravascular mass of proteins 3.09 (2.45-4.01) g/kg BW and 3.75 (3.31-4.67) g/kg BW. All differences were statistically significant at least on the 5% level. The physiological consequences for athletes of having a lower hematocrit and lower protein concentration but a higher intravascular mass of proteins (+22%) for their water balance as well as for their dietary protein intake are discussed. Endurance exercise stimulates mainly the synthesis of albumin and globulins produced by the liver resulting in an expansion of the PV. The protein synthesis of the RES does not seem to respond to exercise stimulus.

**291. Röcker, L., K.A. Kirsch, and H. Stoboy:**

Sex-dependent changes in plasma globulins in women and men exposed to heat stress.

*Israel Journal of Medical Sciences* 14:212-217, 1978.

**Authors' abstract**

Healthy, sedentary women and men, aged 20 to 30 years, were exposed to the same degree of intermittent heat stress in a sauna bath. Blood samples were taken immediately before and at various intervals after heat exposure. The concentrations and intravascular masses of IgG, IgA, IgM,  $\alpha_1$ -antitrypsin, transferrin and  $\alpha_2$ -macroglobulin were determined by the radial immunodiffusion technique and by the measurement of plasma volume. Losses in body weight and plasma volume were lower in women than in men. The globulin concentrations increased significantly in both sexes after heat exposure. The sum of the masses of individual globulins increased only in women, a change interpreted as globulin shifts from the interstitial into the vascular space. Whereas it is unlikely that sex-dependent differences in these shifts are due to changes in vascular permeability, it seems that the protein composition of the lymphatic fluid entering the vascular space plays an important role in these shifts.

**292. Rodriguez, A.B., C. Barriga, and**

**M. De la Fuente:**

Phagocytic function of blood neutrophils in sedentary young people after physical exercise.

*International Journal of Sports Medicine* 12:276-280, 1991.

**Authors' abstract**

The effect of exhaustive exercise on the phagocytic function of blood polymorphonuclear neutrophils in sedentary men and women has been studied. Adherence capacity to the endothelium, spontaneous mobility, chemotaxis and ingestion of *Candida albicans* were not modified after physical exercise. However, opsonization

of *Candida albicans* as well as candidicide power increased significantly in men and women after exercise. The immediate advantages of physical exercise on the phagocytic immune response is discussed.

**293. Rosenbaum, H.E. and C.G. Harford:**

Effect of fatigue on susceptibility of mice to poliomyelitis.

*Proceedings of the Society for Experimental Biology and Medicine* 83:678-681, 1953.

**Authors' abstract**

In order to determine the effect of fatigue on susceptibility to experimental poliomyelitis, mice were forced to run in a revolving drum during the day preceding and for 8 hours each day subsequent to the intracerebral injection of the Lansing strain of virus. Control animals inoculated at the same time with the same amount of virus were allowed to rest in their cages. In all 7 experiments, the incidence of the disease as measured both by paralysis and by death was greater in the exercised animals than in the resting controls.

**294. Rusch, H.P. and B.E. Kline:**

The effect of exercise on the growth of a mouse tumor.

*Cancer Research* 3:116-118, 1943.

**Synopsis**

**Purpose** To test the influence of forced exercise on the rate of tumor growth of mice bearing transplantable tumors.

**Methods**

1. Albino mice were placed in a motor-driven rotating cage and subjected to forced exercise for a period preceding and following inoculation with a transplantable fibrosarcoma.

2. The rate of growth of the tumors was then compared to a control group receiving the same daily caloric equivalent of food, but not subjected to forced exercise.

**Results**

1. The exercised mice gained less weight and the rate of tumor growth was less than that observed in the control group.

**Conclusions**

1. These data support a caloric effect on reducing tumor growth.

2. The effect can also be demonstrated by changing the caloric requirements of mice while maintaining constant dietary intake.

### 295. Russell, W.R.:

Poliomyelitis: The pre-paralytic stage, and the effect of physical activity on the severity of paralysis.  
*British Medical Journal* 2:1023-1028, 1947.

#### Author's abstract

Forty-four patients convalescent from poliomyelitis, who were old enough to describe their symptoms, were questioned at length regarding their early symptoms and also the amount of physical activity during the early days of the disease. The so-called meningitic symptoms appear in nearly all cases during the pre-paralytic stage of the disease and are of great value in diagnosis. These symptoms are often more suggestive of involvement of nerve roots than of meninges. They consist of pain in the head, neck, dorsal, lumbar, or sacral spine, scapular region, thighs, or the lower chest. The meningitic symptoms may be slight or severe. At their onset the patient may be afebrile and may feel quite well. The meningitic symptoms may abate and the patient feel better shortly before paralysis develops. Physical activity of any kind during the pre-paralytic stage increases the danger of severe paralysis. Complete physical rest in bed during the whole of the pre-paralytic stage seems to protect the patient from severe paralysis.

### 296. Russell, W.R.:

Paralytic poliomyelitis: The early symptoms and the effect of physical activity on the course of the disease.

*British Medical Journal* 1:465-471, 1949.

#### Author's abstract

In 100 cases of poliomyelitis the early symptoms have been studied in detail. The prodromal stage, when present, consists usually of a brief non-specific illness, but neurological symptoms occasionally appear even at this early stage. The pre-paralytic stage is the most critical period of the disease. Spinal symptoms in "typical" cases begin abruptly, and occurred in 95 of the 100 cases. They are of great value in diagnosis, but are very variable as regards both type and severity. Two or more phases of the pre-paralytic stage may appear, and paralysis may spread in two or more stages. The spinal symptoms may subside before paralysis develops. In "atypical" cases the onset of the pre-paralytic stage is vague, and the symptoms of a prodromal stage may appear to merge into the pre-paralytic stage. An unusual amount of physical activity

immediately preceded the pre-paralytic stage in 14 of 100 cases. Complete physical rest in bed from the onset of the pre-paralytic stage greatly reduces the danger of severe paralysis. Severe physical activity at this stage is almost suicidal, while the continuance of even average physical activity is dangerous. The possible effect of trauma in localizing the disease is considered. During an epidemic physical activity should be avoided entirely in minor illnesses. The highly dangerous belief that malaise and other vague symptoms should be "worked off" by exercise requires correction.

### 297. Sawka, M.N., A.J. Young, R.C. Dennis, R.R. Gonzalez, K.B. Pandolf, and C.R. Valeri:

Human intravascular immunoglobulin responses to exercise-heat and hypohydration.

*Aviation, Space and Environmental Medicine*  
60:634-638, 1989.

#### Authors' abstract

Several investigators have suggested that prolonged exercise and hypohydration alter the intravascular mass of immunoglobulins. Those studies, however, have methodological concerns which make generalizations from their data very tenuous. This study examined the effect of prolonged moderate intensity exercise in the heat and hypohydration on changes in the intravascular mass of immunoglobulins. Five heat-acclimated males attempted two Heat Stress Tests (HSTs). One HST was completed when subjects were euhydrated and the other HST when subjects were hypohydrated (~5% from base line body weight). The HSTs consisted of 30 min of rest in a 20°C antechamber, followed by a 120-min exposure (2 repeats of 15 min rest and 45 min walking) in a hot (35°C, 45% rh) environment. The following observations were made concerning immunoglobulin responses to hypohydration and exercise-heat stress: a) the changes in concentrations ( $\text{mg}\cdot\text{dl}^{-1}$ ) of the measured immunoglobulins were often a reflection of the changes in the plasma volume; b) hypohydration increased the intravascular mass (g) of the complement enzyme C3 during resting conditions, but did not alter the intravascular mass of IgG, IgA, and IgM; and c) prolonged treadmill exercise in the heat, when either euhydrated or hypohydrated, did not alter the intravascular mass of IgG, IgA, IgM, and C3. These data indicate that the intravascular mass of immunoglobulins does not change during prolonged moderate intensity exercise in the heat, and that hypohydration results in a translocation of C3 to the intravascular space. In addition, these data indicate that immunoglobulins do not provide a stress index for hypohydration.

**298. Schaefer, R.M., K. Kokot, A. Heidland, and R. Plass:**

Jogger's leukocytes.

*New England Journal of Medicine* 316:223-224, 1987.

**Authors' abstract**

Recently, we conducted a study to evaluate the effect of physical exercise on the activation of polymorphonuclear leukocytes. As a measure of leukocyte activation, the release of polymorphonuclear elastase was determined. Plasma levels of polymorphonuclear elastase were measured in complex with  $\alpha_1$ -proteinase inhibitor (E- $\alpha_1$ -PI) with use of an enzyme immunoassay. Ten healthy male subjects with an interest in jogging underwent both short-term exercise (running 2000 m) and long-term exercise (running 10,000 m). Blood samples were obtained immediately after exercise. After short-term

exercise, the number of circulating leukocytes increased from  $6470 \pm 500$  to  $7820 \pm 530$  per microliter, and there was a small (16 percent) increment in the plasma levels of E- $\alpha_1$ -PI (table 1). On the other hand, long term exertion caused a significant leukocytosis, with an increase of  $6020 \pm 640$  to  $9670 \pm 860$  leukocytes per microliter, and a marked increase of E- $\alpha_1$ -PI in the plasma (186 percent), suggesting that this compound was released by degranulation of neutrophils during prolonged physical activity (table 1).

These results indicate that exercise causes not only an increase in the number of leukocytes but also an increment in the activity of these cells. It is noteworthy that particularly high plasma levels of E- $\alpha_1$ -PI have been observed during bacterial infections. Thus, this response of polymorphonuclear leukocytes to physical exercise is similar to an infectious or inflammatory challenge.

**Table 1. Effects of physical exercise on plasma levels of elastase- $\alpha_1$ -proteinase inhibitor complex (E- $\alpha_1$ -PI) in 10 subject\***

	Level of E- $\alpha_1$ -PI	
	Short-term	Long-term
	ng/ml	
Before exercise	$100 \pm 4$ (85-113)	$106 \pm 9$ (88-115)
After exercise	$116 \pm 12$ (97-134)	$303 \pm 23$ (246-351)
P value	NS	$\leq 0.001$

\*Plus-minus values are means  $\pm$  SEM, and values in parentheses are ranges. The significance of differences before and after exercise was tested by the Mann-Whitney test; NS denotes not significant.

**299. Schlenzig, C., H. Jäger, and H. Rieder:**

Einfluss von Sporttherapie auf die zelluläre Immunabwehr und die Psyche HIV-infizierter Männer. *Deutsche Zeitschrift für Sportmedizin* 41:156-160, 1990.

**Authors' abstract**

The influence of supervised therapeutic physical exercise of eight weeks' duration on the cellular immune system and the psychological situation in HIV-antibody (AB)-positive individuals were investigated in a controlled prospective study. Twenty-eight HIV-AB-positive male patients were stratified according to the Walter-Reed-Staging Classification (Stages 1 through 4 were induced). Fifteen subjects were randomly assigned to participate in one-hour endurance exercise sessions twice a week over a period of 8 weeks. The control group of 13 patients did not receive exercise treatment. Within the first 4 weeks the number of CD4<sup>+</sup> cells increased in 67% of the subjects receiving therapy, as compared to 58% in the control subjects. The CD4<sup>+</sup>/CD8<sup>+</sup> ratio of the test group increased from 0.45 to 0.47, while the ratio in the control subjects decreased from 0.49 to 0.43. In addition, delayed cutaneous hypersensitivity reactions, measured by recall antigens (Multitest Mérieux), increased (from 12.8/2 to 16.2/3). Considering a lack of psychological changes, the items depression, fatigue, vigor, and anger of the standardized psychological test POMS showed a correlation with immunological parameters. These results demonstrate that carefully directed exercise can improve the cellular immune system as well as the psychological situation in HIV-infected males.

**300. Schneider, E.C. and L.C. Havens:**

Changes in the blood after muscular activity and during training. *American Journal of Physiology* 36:239-259, 1914-1915.

**Authors' abstract**

1. The immediate influence of physical exertion upon the blood of the peripheral capillaries was one of concentration in which the percentage of increase varied as follows: haemoglobin 3.5 to 10.9, erythrocytes 3.2 to 22.8, and leucocytes 13.8 to 130.2. The specific gravity increased proportionately with the red corpuscles.
2. Within a few minutes after the close of the exertion the blood began to be diluted and this usually resulted in a sub-normal specific gravity and content of haemoglobin and red corpuscles.
3. At the end of the exertion the differential counts of the leucocytes showed no change, but very soon the

polymorphonuclears increased 9 to 45% and the total number of mononuclear elements decreased 14 to 55%.

4. The number of platelets was unchanged at the close of the exercise. However, there then followed a period of decrease which reduced them 17 to 30%. Later there was a period of overproduction which carried the number above the normal 17 to 25%.
5. Long continued and severe exertion apparently does not cause an increased destruction of red corpuscles.
6. A repetition of a run when the blood has passed into the subnormal condition practically restores the maximum concentration.
7. Abdominal massage and pressure raise the content of haemoglobin and red corpuscles in the peripheral capillaries.
8. A tightly drawn belt or pressure on the abdomen following exertion prevents in large measure the dilution of the blood.
9. At an altitude of 14,109 feet the blood does not concentrate during exercise. However, the changes in white corpuscles and platelets occur as at lower altitude.
10. Abdominal massage and compression cause a dilution of the blood at high altitude.
11. Adrenalin administered by mouth causes the blood in the peripheral capillaries to be concentrated.
12. During a period of training for spring athletics the percentage and the number of red corpuscles were found to increase. The number of leucocytes and platelets was not changed. The mononuclear elements were increased 4.1%. No change in total oxygen capacity or total blood volume was found.

**302. Schouten, W.J., R. Verschuur, and**

**H.C.G. Kemper:**

Habitual physical activity, strenuous exercise, and salivary immunoglobulin A levels in young adults: The Amsterdam Growth and Health study. *International Journal of Sports Medicine* 9:289-293, 1988.

**Authors' abstract**

Secretory IgA (S-IgA) levels in stimulated saliva were measured before and after a maximal treadmill test in a population of 175 young adults (84 men, 91 women). Habitual physical activity levels of this population were measured by a standardization interview, and scores were obtained for the amount of time and intensity of sports activities and total activity. Before the maximal treadmill

test, men and women showed no statistically significant differences in the salivary concentrations of S-IgA, but the concentration of S-IgA in women decreased and in men increased statistically significantly ( $P < 0.05$ ) after the treadmill test. Only women showed a significant correlation between absolute values of S-IgA and the weekly amount of time spent on sports activity measured by a standardization interview expressed in minutes per week.

### 303. Schouten, W.J., R. Verschuur, and H.C.G. Kemper:

Physical activity and upper respiratory tract infections in a normal population of young men and women: The Amsterdam Growth and Health study. *International Journal of Sports Medicine* 9:451-455, 1988.

#### Authors' abstract

A population of young adults, 92 men and 107 women, with a mean age of 21 ( $\pm 0.7$ ) years, were retrospectively questioned about their habitual physical activity levels (period of 3 months) and the incidence and duration of upper respiratory tract infection (URI) symptoms (period of 6 months). We hypothesized that the incidence and duration of URI symptoms were inversely related with the level of sports activity and total physical activity. Only in women was a statistically significant ( $P < 0.05$ ) negative relation found between the incidence of URI symptoms and the level of sports activity. However, the low Spearman's rho coefficient ( $-0.18$ ) indicates a very weak relation between both parameters.

### 304. Seneczko, F.:

White blood cell count and adherence in sportsmen and non-training subjects. *Acta Physiologica Polonica* 34:601-610, 1983.

#### Author's abstract

The white blood cell count and differential white blood cell count as well as the adherence of these cells were determined in 31 young clinically healthy men not participating actively in any sports and in 32 footballers belonging to third league sports clubs. In the group of footballers the determinations were carried out twice: in the initial period and then at the end of the highest-form period of the one-year training cycle. In the footballers in relation to the control group the total white blood cell count was raised, the differential count showed a shift in favour of neutrophils, eosinophils and monocytes at the expense of lymphocytes. The lymphocyte adherence was significantly decreased.

### 305. Seneczko, F. and B. Rzetelski:

Limfocyty TiB krwi obwodowej w roznych okresach rocznego cyklu treningowego pilkarzy i osob nietrenujacych. (Peripheral blood T and B lymphocytes at various phases of an annual training cycle in soccer players and non-training persons). *Immunologia Polska* 9:197-205, 1984.

#### Authors' abstract

T and B lymphocyte numbers were estimated at two phases of an annual training cycle in 32 third-league soccer players with training experience of 3 to 15 years, and in 31 college students exercising exclusively during school classes of physical education. As compared to the control group, the sportsmen exhibited lowered numbers of lymphocytes T (particularly at the end of their top physical condition period) and lowered numbers of lymphocytes B (particularly at the beginning of their top physical condition period).

### 306. Severson, R.K., A.M.Y. Nomura,

J.S. Grove, and G.N. Stemmermann:

A prospective analysis of physical activity and cancer.

*American Journal of Epidemiology* 130:522-529, 1989.

#### Authors' abstract

Previous studies have suggested that increased physical activity may be protective against colon cancer. Most of these studies measured activity indirectly. The present study evaluated several direct measurements of physical activity and also resting heart rate as determined from electrocardiogram. Increased activity was consistently associated with a decreased relative risk of colon cancer for each measure of activity. The colon cancer relative risk estimates for the middle and upper tertiles of a physical activity index (compared with the lower tertile) were 0.56 (95% confidence interval (CI) 0.39-0.80) and 0.71 (95% CI 0.51-0.99), respectively. Relative risk of colon cancer associated with moderate or heavy activity at home/recreation (compared with mostly sitting) was 0.66 (95% CI 0.49-0.88). A similar comparison of activity at work resulted in a relative risk estimate of 0.72 (95% CI 0.52-1.00). Relative risk of colon cancer increased significantly ( $p = 0.027$ ) with increasing resting heart rate. Relative risks associated with physical activity were also evaluated for cancers of the stomach, rectum, lung, prostate, and urinary bladder. An increased relative risk of stomach cancer was associated with several measures of increased activity, but these results are preliminary and additional research is necessary to further evaluate this finding.

**307. Shechtman, O., R. Elizondo, and M. Taylor:**

Exercise augments interleukin-2 induction.  
*Medicine and Science in Sports and Exercise* 20:S18, 1988.

**Authors' abstract**

The purpose of this study was to determine whether acute exercise enhanced Interleukin-2 (IL-2) induction, and whether core temperature ( $T_c$ ) was a factor in the above response. Eight men exercised on a bicycle ergometer at 60%  $\dot{V}O_2$  max for 1 hour, and on a different day underwent passive heating until  $T_c$  matched that of exercise. Venous blood was sampled before, during and 30 minutes after exercise and heating. The white blood cells (WBC) were separated and incubated with mitogen. WBC supernatant was collected 49 hours post incubation, and measured for IL2 activity. IL2 levels for the exercise test were 1.6, 2.3, and 2.1 units/ml and for heating 2.4, 3.2, and 2.9 units/ml, for rest, experiment and recovery, respectively. IL2 levels were significantly higher ( $P < 0.05$ ) during exercise and heating when compared to resting levels. Exercise enhanced IL2 induction by 44% above resting levels, and heating by 30%. The recovery IL2 levels were still elevated (31% and 21% for exercise and heating, respectively). The data suggests that exercise may stimulate natural immunity, and that elevated  $T_c$  may partially account for the enhanced IL2 induction. Blood levels of catecholamines increased more with exercise than with heating, suggesting a possible role of these hormones in augmenting *in vivo* IL2 induction.

**308. Sheffer, A.L. and K.F. Austen:**

Exercise-induced anaphylaxis.  
*Journal of Allergy and Clinical Immunology* 66:106-111, 1980.

**Authors' abstract**

Sixteen patients were seen because of possibly life-threatening exercise-associated symptoms similar to anaphylactic reactions. Asthma attacks, cholinergic urticaria and angioedema, and cardiac arrhythmias are recognized as exertion-related phenomena in predisposed patients but are distinct from the syndrome described here. A syndrome characterized by the exertion-related onset of cutaneous pruritus and warmth, the development of generalized urticaria, and the appearance of such additional manifestations as collapse in 12 patients, gastrointestinal tract symptoms in five patients, and upper respiratory distress in 10 patients has been designated exercise-induced anaphylaxis, because of the striking similarity of this symptom complex to the anaphylactic syndrome elicited by ingestion or injection of a foreign

antigenic substance. There is a family history of atopic disease for 11 patients and cold urticaria for two others and a personal history of atopy in six. The size of the wheals, the failure to develop an attack with a warm bath or shower or a fever, and the prominence of syncope rule against the diagnosis of conventional cholinergic urticaria. There is no history or evidence of an encounter with an environmental source of antigen during the exercise period.

**309. Shephard, R.J., T.J. Verde,**

**S.G. Thomas, and P. Shek:**

Physical activity and the immune system.  
*Canadian Journal of Sport Sciences* 16:163-185, 1991.

**Authors' abstract**

Methods of examining the immune function include a charting of susceptibility to infections, differential blood counts or lymphocytes counts, and measures of cell proliferation and immunoglobulin synthesis in response to external mitogens. The reported acute response to exercise is transient and quite variable, depending upon the type of exercise, the immunological methodology used, the intensity of effort relative to the fitness of the individual, and the timing of observations. A leucocytosis, a granulocytosis, a small lymphocytosis, and a decrease in the proportion of T to B cells reflect mainly changes of blood volume, demargination, and migration of cells. Lymphocyte subsets show a decreased helper/suppressor cell ratio and an increase of natural killer cells. Because of the lymphocytosis, mitogens induce an increased overall cell proliferation, but proliferation for a given number of cells is decreased. Prolonged exercise leads to a decrease of serum and salivary immunoglobulin levels. Soluble factors such as interleukin-1 and interferon are increased by a bout of exercise. Cross-sectional comparisons and training experiments suggest that under resting conditions well-conditioned individuals show some lymphocytosis, increased natural killer cell activity, higher levels of interleukin-1, and possibly an enhanced reactions to mitogens. Moderate training does not greatly change exercise responses at a given fraction of maximal effort. Excessive training suppresses immune function, but their changes are small, variable, and thus difficult to relate to overtraining. Moreover, because of their transient nature, they have only a limited influence upon the risks of infection or cancer.



- 310. Shoenfeld, Y., D. Aloni, G. Keren, M. Shaklai, M. Djaldetti, and J. Pinkhas:**  
Effect of physical effort on the white blood cells in benign familial leukopenia.  
*Acta Haematologica* 65:108-113, 1981.

**Authors' abstract**

The components of the peripheral white blood cells (WBC) were determined before and after 10 min of submaximal ergometric work in two groups of subjects: 34 healthy Yemenite Jews with benign familial leukopenia (BFL) and 34 healthy Yemenite Jews without BFL. The mean  $\pm$  SEM of the increase in the peripheral WBC following the effort in the control group was  $2,606 \pm 1,272$  cells/mm<sup>3</sup>, due to the relative rise in the neutrophils, eosinophils, monocytes, and lymphocytes. The identical ergometric work, performed by BFL subjects, brought about a significantly lower increase ( $700 \pm 865$  cells/mm<sup>3</sup>) in the peripheral WBC, the majority of which were lymphocytes. It seems that subjects with this form of BFL lack granulocytes in the marginal pool.

- 311. Shubik, V.M., V.N. Pulkov, and**

**N.I. Mashneva:**

Immunological parameters following physical exercise. (In Russian).

*Gigiyena i Sanitariya* 7:39-41, 1986.

**Author's summary**

White mice were chronically exposed to a combination of <sup>90</sup>SR, stable lead and exercises of different intensity. Moderate-intensity exercises were found to stimulate and normalize some parameters of humoral nonspecific defense and immunity. More intensive exercise associated with stress (running in a drum, swimming) may lead to immunological impairments.

- 312. Simon, H.B.:**

The immunology of exercise: A brief review.  
*Journal of the American Medical Association* 252:2735-2738, 1984.

**Author's abstract**

Many athletes believe that habitual exercise protects them against infection. This article reviews ten studies of the effects of exercise on various host-defense factors. Exercise produced a transient granulocytosis and lymphocytosis, and in some studies, lymphocyte function was reported to have been enhanced. Serum immunoglobulin and complement levels were not significantly altered in the small number of subjects studied. Two recent studies

showed that exercise produced an increase in circulating endogenous pyrogen in man. Since it now appears that endogenous pyrogen is identical to interleukin-1, a product of mononuclear cells that enhances lymphocyte function, it may play a role in host defense. Further studies will be needed before it can be concluded that exercise effects the host response to infection in any clinically meaningful way.

- 313. Simon, H.B.:**

Exercise and infection.

*The Physician and Sportsmedicine* 15:135-141, 1987.

**Author's abstract**

Many athletes believe that exercise improves their resistance to infection, but no epidemiological data support this claim. Studies of various host defense mechanisms have produced inconclusive results. Transient lymphocytosis and polymorphonuclear leukocytosis occur with exercise, but they may not be functionally significant. Levels of interleukin-1, an immunostimulant, rise with exercise; this area warrants further study. Both athletes and sedentary individuals are subject to the same infections and can be treated in the same way. However, athletes should be cautioned against strenuous exertion when they are febrile or systemically ill, and should substitute gentle stretching exercises until they have recovered.

- 314. Simpson, J.R., and L. Hoffman-Goetz:**

Exercise stress and murine natural killer cell function.

*Proceedings of the Society for Experimental Biology and Medicine* 195:129-135, 1990.

**Authors' abstract**

Male C3He mice were trained to run on a treadmill (final speed, slope and duration of 30 m/min, 8 degrees, 30 min/day, 5 days/week, respectively) for 10 weeks or they remained sedentary. At the end of the training program, half of the mice were sacrificed and half were given a single bout of exercise to exhaustion (50% stepwise increases in final running speed for 2-min intervals). Splenic catecholamine concentrations, splenic natural killer cell cytolytic activity against YAC-1 tumor targets, and frequency of asialo GM<sub>1</sub> (a murine natural killer cell surface glycolipid)-positive splenocytes were assessed. Exhaustive exercise in both trained and untrained mice reduced the in vitro killing of tumor targets by splenic natural killer cells relative to killing by splenocytes from mice which did not undergo the acute exercise bout ( $P < 0.05$ ). The frequency of asialo

GM<sub>1</sub>-positive splenocytes was also reduced in the exhaustively exercised animals ( $P < 0.05$ ). Training alone, without the additional stress of exhaustive exercise, reduced the frequency of asialo GM<sub>1</sub> positive splenocytes relative to a sedentary condition ( $P < 0.05$ ), but did not compromise natural killer cell cytolytic activity against the tumor targets. Splenic epinephrine concentrations in the exhaustively exercised animals were elevated 3- to 5-fold above the concentrations observed in trained and sedentary mice. These results suggest that a single, acute exercise bout reduces the capacity of splenic natural killer cells to kill tumor targets in vitro and that training enhances splenic natural killer cell cytolytic activity, on a per cell basis, against tumor targets.

### 315. Simpson, J.R., and L. Hoffman-Goetz:

Exercise, serum zinc, and interleukin-1 concentrations in man: Some methodological considerations.

*Nutrition Research* 11:309-323, 1991.

#### Authors' abstract

The effects of four cycle ergometry exercise sessions of varying intensity and duration in men of low, moderate, and high fitness levels on serum zinc (Zn) concentrations were studied. Interleukin 1 (IL-1) concentrations were determined in highly fit men for high intensity exercise. Control subjects, who did not exercise, were sampled concurrently to determine diurnal changes in serum zinc concentrations. Serum Zn concentrations dropped significantly ( $p < 0.05$ ) in all fitness groups two hours after both 30 minutes and 120 minutes of exercise at 65% of maximal oxygen uptake ( $\dot{V}O_2$  max) relative to basal (pre-exercise) values. This effect was not different from the diurnal variation in the controls. When serum Zn concentrations were adjusted for concomitant plasma volume changes, the diurnal effects observed for low and moderately fit subjects disappeared two hours after work at 65% of  $\dot{V}O_2$  max. Two hours of exercise at 65%  $\dot{V}O_2$  max resulted in a significant reduction ( $p < 0.01$ ) in serum Zn concentrations 24 hours after completion of the exercise bout in men of moderate and high fitness levels. Serum Zn concentrations decreased two hours after 60 minutes of exercise of high intensity (75% of  $\dot{V}O_2$  max) for all fitness groups relative to controls; these effects, however, were abolished upon adjustment for plasma volume changes. There was no effect on serum Zn of 60 minutes of exercise at low intensity (30%  $\dot{V}O_2$  max). Serum IL-1 concentrations were unchanged two hours after 60 minutes of exercise at 75% of  $\dot{V}O_2$  max in highly fit subjects relative to basal level and to control values. These data suggest that: 1) the changes in serum Zn concentrations with exercise need to be

considered vis-a-vis the diurnal pattern of serum Zn fluctuations and transitory changes in plasma volume; 2) the effect of cycle ergometry exercise on serum Zn concentrations is modified by duration, but not intensity, of exercise; and 3) fitness plays a minor, but not significant, role in the response of concentrations of Zn in serum to exercise.

### 316. Simpson, J.A.R., L. Hoffman-Goetz, R. Thorne, and Y. Arumugam:

Exercise stress alters the percentage of splenic lymphocyte subsets in response to mitogen but not in response to interleukin-1.

*Brain, Behavior, and Immunity* 3:119-128, 1989.

#### Authors' abstract

Results of previous work from this laboratory demonstrated that reduced murine splenic lymphocyte proliferation in response to Concanavalin A (Con A) is associated with acute exercise stress. The present study was conducted to determine whether the stress of physical work further affects the expression of splenic lymphocyte phenotypes following in vitro stimulation by the T-cell mitogen, Con A, and also by interleukin-1 (IL1). Mice in this study were assigned to one of five treatment conditions. Two groups of mice were exposed only to the noise and vibration of a treadmill for 8 weeks; one of these groups was given an acute exhaustive run. Three groups of mice were exposed to 8 weeks of treadmill training: one group was sacrificed immediately after training, a second group was sacrificed 72 h after training, and a third group was rested for 72 h and then given an acute exhaustive run. There was a significant effect of stimulation by Con A on the percentage of splenic lymphocytes positive for Thy 1.2, Lyt-2, L3T4, and goat anti-mouse Ig, regardless of treatment condition. Acute exercise, however, affected the magnitude of the response. There was a significantly greater increase in the percentage of Thy 1.2+ and, especially of, Lyt-2+ cells in stimulated splenic lymphocytes from untrained mice given an exhaustive exercise session compared with controls and with trained mice. There was no significant effect of the addition of IL1 to any culture, irrespective of treatment condition. These results suggest that reduced mitogenesis after acute exercise stress exposure may be related to the increased appearance of Lyt-2+ (T suppressor) cells.

317. Simpson-Westenberg, M., D.C. Nieman, W.S. Youngberg, K. Arabatzis, W.C. Eby, S.A. Tan, J.W. Lee, and L.S. Berk:

The effect of long endurance running on natural killer cell activity in experienced marathoners.

*Medicine and Science in Sports and Exercise* 21:S109, 1989.

**Authors' abstract**

Ten experienced marathoners were exercised 3-h to exhaustion in the laboratory. Blood samples were collected at baseline, 1-h exercise and 5-min., 6-h, and 21-h recovery, and analyzed for changes in natural killer (NK) activity and total number of lymphocytes expressing membrane receptors for NK markers. Using repeated measures ANOVA all of the NK markers except for Leu7<sup>+</sup>2<sup>+</sup>, Leu7<sup>+</sup>11<sup>-</sup>, and Leu7<sup>+</sup>11<sup>+</sup> showed significant within subject effects over time. Simple contrasts with baseline values showed that at 1.5-h recovery, total number of lymphocytes bearing 4 different markers, Leu11<sup>+</sup> 19<sup>+</sup>, Leu11<sup>+</sup>19<sup>-</sup>, Leu7<sup>+</sup>11<sup>-</sup>, and Leu11<sup>+</sup>7<sup>-</sup>, were significantly decreased when compared with baseline values. Three of these 4 (all except Leu7<sup>+</sup>11<sup>-</sup>) were still significantly below baseline levels by 21-h recovery. At 1.5-h recovery, NK activity was significantly decreased below baseline levels when using 4 of the 6 effector cells/target cell (EC:TC) ratios. By 6-h recovery, NK activity was still decreased significantly when using 12.5:1 and 3.13:1 EC:TC ratios. By 21-h recovery, NK cell activity was back to baseline levels. Cortisol levels at 5-min post exercise were negatively correlated with NK activity at 1.5-h recovery ( $r = -0.66$ ,  $P = 0.04$ , 25:1 EC:TC;  $r = -0.62$ ,  $P = 0.05$ , 50:1 EC:TC). NK cells are involved along with response and partial control of bacteria and viruses. The decrease in NK activity found in this study following a 3-h run which was paralleled by decrease in 4 of 7 NK cell markers suggests a negative effect on host protection following marathon events.

318. Siscovick, D.S., R.E. Laporte, and J.M. Newman:

The disease-specific benefits and risks of physical activity and exercise.

*Public Health Reports* 100:180-188, 1985.

**Authors' summary:**

Physical inactivity has been related to the occurrence of coronary heart disease, hypertension, diabetes mellitus, and osteoporosis. The literature was reviewed to determine what is and what is not known about the efficacy and safety of physical activity in each of these conditions.

Although there is a transient increase in the risk of sudden cardiac death during vigorous activity, there is mounting evidence that habitual vigorous activity is associated with an overall reduced risk of coronary heart disease. It is unlikely that this association merely reflects the "selection" that results from sick persons who tend to be less active. Several studies suggest that physical activity may be related to the prevention and control of hypertension, diabetes mellitus, and osteoporosis. However, additional research is needed to make explicit the risks and benefits of physical activity in each of these conditions. Finally, future efforts should determine the type, intensity, frequency, and duration of activity required to maximize the benefits and minimize the hazards of physical activity. The public health and clinical significance of these questions requires that they be examined in the most rigorous manner feasible.

319. Smith, J.A., R.D. Telford, I.B. Mason, and M.J. Weidemann:

Exercise, training and neutrophil microbicidal activity.

*International Journal of Sports Medicine* 11:179-187, 1990.

**Authors' abstract**

The concentration in human plasma of putative neutrophil-"priming" cytokines like endogenous pyrogens is known to increase significantly in response to moderate exercise. This is characteristic of an acute-phase response. The ability of blood neutrophils isolated from both trained and untrained human subjects ( $n = 11$ , 9) to produce microbicidal reactive oxygen species was determined using luminol-enhanced chemiluminescence both before and after one hour of aerobic exercise at 60%  $\dot{V}O_2$  max. Irrespective of training and stimulus concentration, exercise nearly always caused a significant "priming" of the capacity of neutrophils to produce  $H_2O_2$  and HOCl upon stimulation with opsonized zymosan ( $P < 0.01$ ); however, compared to their untrained counterparts, the activity of cells isolated from trained individuals was depressed about 50% at unit stimulus concentration, both before and after exercise ( $P < 0.075$ ), whilst remaining unaltered at saturating concentrations. Although neutrophil oxygenation activity is only one parameter that contributes to immunological status, regular episodes of moderate exercise may increase resistance to infection by priming the "killing capacity" of neutrophils. In contrast, prolonged periods of intensive training may lead to increased susceptibility to common infections by diminishing this activity.

**320. Smith, J.K., D.S. Chi, G. Krish,**

**S. Reynolds, and G. Cambron:**

Effect of exercise on complement activity.

*Annals of Allergy* 65:304-310, 1990.

**Authors' abstract**

Complement measurements of C1, C1q, C2, C3, C4, C5; the anaphylatoxins, C3a, C4a, and C5a; and total hemolytic activity of the classical and alternative pathways were made in 26 experienced adult runners before and after short-term aerobic exercise. The baseline results were compared with those of nonexercising age-matched controls. In most subjects tested, running resulted in nanogram increases in C3a and C4a with corresponding decreases in the hemolytic activity of C4 (C4H). Baseline values of C3 and C4H were decreased significantly in runners when compared with nonexercising controls. Preliminary studies measuring the effect of exercise on C3a levels were also done in three asthmatic runners. Mean resting and postexercise levels, and exercise-induced increases in C3a anaphylatoxin in the asthmatic subjects were significantly higher than in the non-asthmatic subjects. The findings indicate that short-term exercise results in the activation of C3 and C4 and subsequent generation of C3a and C4a anaphylatoxins, and suggest that both activation of the classical pathway of complement and a selective downregulation of C3 production may occur in persons regularly engaged in aerobic exercise. The exaggerated generation of C3a by asthmatic subjects during exercise raises the possibility that anaphylatoxins play an etiologic role in exercise-induced asthma.

**321. Solomon, G.F.:**

Psychosocial factors, exercise, and immunity:

Athletes, elderly persons, and AIDS patients.

*International Journal of Sports Medicine*

12:S50-S52, 1991.

**Author's abstract**

Maximal bicycle ergometry exercise increases natural killer (NK) cell activity and numbers in both healthy old and young persons to equivalent degree but with great variability in the old. Exercise-induced increase in NK activity, but not numbers, is blocked by the opioid antagonist naloxone. Lactating females do not show exercise-induced augmentation of NK cell activity. A predisposition to autoimmune disease, particularly rheumatoid arthritis, may exist among athletes, and disease may ensue when athleticism ceases. Long-term survivors with AIDS generally engage in physical fitness/exercise programs.

**322. Soppi, E., P. Varjo, J. Eskola, and**

**L.A. Laitinen:**

Effect of strenuous physical stress on circulating lymphocyte number and function before and after training.

*Journal of Clinical and Laboratory Immunology*

8:43-46, 1982.

**Authors' abstract**

Seventeen young male subjects underwent a six-week training period and their physical fitness was examined using a bicycle ergometer test. Twelve subjects without any marked training served as controls. Venous blood was drawn immediately before and after exercise on a bicycle ergometer both before and after training. After exercise, the subjects developed a leukocytosis as well as lymphocytosis where the proportion of E-rosettes, theophylline resistant E-rosettes and SIg-positive cells remained stable but their absolute number rose by more than 100% before training and more than 50% after training. In spite of the rise of immunocompetent cells in the circulation, the post exercise increase of lymphocyte transformation was not more than 10% both before and after training. After training the response to physical stress is manifested by a significantly weaker mobilization of lymphocytes into the circulation than before training. Consequently, when physical fitness is high fewer immunocompetent cells are required to produce a normal immune response than when physical fitness is low. Our findings indicate that in healthy individuals improved physical fitness compensates for the influence of stress on the immune system.

**323. Spence, D.W., M.L.A. Galantino,**

**K.A. Mossberg, and S.O. Zimmerman:**

Progressive resistance exercise: Effect on muscle function and anthropometry of a select AIDS

population.

*Archives of Physical Medicine and Rehabilitation*

71:644-648, 1990.

**Authors' abstract**

Substantial body tissue wasting has been reported in acquired immune deficiency syndrome (AIDS) patients. The purpose of this investigation was to determine if progressive resistance exercise (PRE) would improve muscle function and increase body dimensions and mass in AIDS patients. The subjects were 24 male outpatient volunteers, status posttherapy for acute pneumocystis carinii pneumonia. Subjects were randomly assigned to control (n = 12) or experimental (n = 12) subsets. All subjects underwent muscle function testing on

12 variables of torque, force, power, and work; three variables of anthropometry were assessed. The experimental group engaged in PRE three times per week for six weeks. The control group did not exercise beyond their usual daily living activities. Both groups were retested at the end of six weeks. In comparison to the control group, the experimental group significantly increased in 13 of the 15 study variables. Thus, during the nonacute stage of AIDS, physiologic adaptation occurred that improved muscle function and increased body dimensions and mass.

### 324. Stephenson, L.A., M.A. Kolka, and J.E. Wilkerson:

Effect of exercise and passive heat exposure on immunoglobulin and leukocyte concentrations.  
In: *Exercise Physiology: Selected Research*, edited by C.O. Dotson, and J.H. Humphrey. New York: AMS Press, Inc., 1985. p. 145-157.

#### Authors' abstract

Five adult males participated in three experiments in which core temperature ( $T_{re}$ ) and venous plasma immunoglobulin (Ig) concentrations, leukocyte counts, and differentials were determined. In one experiment, the subjects performed maximal exercise to exhaustion (E). In the other two sessions, the six subjects sat in an 80°C sauna for 30 min, without rehydration (PHD) or with rehydration (PHR).  $T_{re}$  increased in all cases (E, +.05°C; PHD, +.09°C; PHR, +1.8°C). A differential decrease in plasma volume was observed in the three procedures (E, -11.2%; PHD, -7.3%; PHR, -3.6%). This hemocentration accounted for the increases in the plasma concentrations of IgG, IgA, and IgM, suggesting that heat stress alone is not a factor in immunoglobulin release. All procedures elicited a leukocytosis (E, +67%; PHD, +16%; PHR, +40%). These data suggest that cardiovascular status and not core temperature is the necessary factor accompanying the leukocytosis of exercise and passive heat stress.

### 325. Stevenson, J.R., D. Kelly, and

#### B. Newberry:

Effects of exercise stress on lymphocyte subpopulations in rats.  
*Federation Proceedings* 45:647, 1986.

#### Authors' abstract

Forced exercise has previously been found to be stressful in rats, increasing plasma corticosterone and depressing immune function. On the other hand, exercise training has lowered corticosterone levels in rats, and we have

reported normalization of response by rat splenocytes to Concanavalin A (Con A) and bacterial lipopolysaccharide (LPS). In this current study, Sprague-Dawley rats were subjected to a one-time continuous 30 min. swim to learn the effects on T-cell subpopulation ratios. Mouse monoclonal antibodies were used to identify the subpopulations among cells obtained at different times after completion of the swim. A significant decline in per cent of T-helper cells out of total cells was found only at 4 hr. after the swim in lymph nodes and thymi, and no change was seen in per cent of T-non-helper cells in any organ. It appears that the single swim session was stressful and that this stress caused depletion of T-helper cells and probably not other T-cells. In another experiment, a single, 12 min. ice water swim was apparently also stressful because it depressed responses of splenocytes to both LPS and Con A.

### 326. Surkina, I.D. and L.V. Kozlovskaya:

Blood leucocytes in sportsmen during adaptation to exercise.

*Laboratornoe Delo* 10:597-601, 1980.

#### Authors' abstract

A group of young figure skaters were examined during training and event periods. A significant decrease in blood leucocyte count was observed during the event stage as compared to the training period: relative and absolute decrease in the number of the eosinophils and segmented neutrophils with a simultaneous increase in the number of the lymphocytes, signs of rejuvenescence of the cells of both the neutrophil and the lymphocytic series, presence of atypical cells such as plasmatic, large hyperbasophilic and blast cells in the peripheral blood in amounts exceeding the normal levels. This suggested that an increase in the proportion of B-lymphocytes in the peripheral blood took place during the event. Correlation between the number of the atypical cells and the preceding training exercise was noted. The data may serve as the basis for special studies on the dynamics of the immunological reactivity in sportsmen at various stages of training.

**327. Swift, W.E., Jr., H.T. Gardner,  
D.J. Moore, F.H. Streiffeld, and  
W.P. Havens, Jr.:**

Clinical course of viral hepatitis and the effect of exercise during convalescence.  
*American Journal of Medicine* 8:614-622, 1950.

**Authors' abstract**

1. Data from 3,614 cases of viral hepatitis in American Occupation forces in Germany, occurring between March 1947 and October 1949, were assembled and analyzed.
2. The course of disease was mild but similar to previous clinical descriptions with the exception of the onset which was insidious and afebrile in a large majority of patients.
3. Since a great many of these patients had much more activity at an earlier phase of convalescence than is usually prescribed without apparent ill effect, an attempt was made to determine the effect of measured exercise on the duration of disease.
4. Thirty-eight patients in various phases of viral hepatitis were given a two week period of graduated exercise and thirty-three similar patients were kept in bed as controls. Twenty-seven other patients did strenuous calisthenics for one day.
5. The mean duration of disease was two weeks longer in patients whose total serum bilirubin measured 3.0 mg. per cent or more at the onset of exercise. The most important indications of an untoward effect of exercise were anorexia, hepatic tenderness or an increase in retention of bromosulfalein.
6. When the total serum bilirubin measured less than 3.0 mg. per cent at the beginning of exercise, the duration of convalescence was apparently not prolonged by exercise as compared with rest in bed, regardless of the age of the patient, severity of disease as measured by the maximum amount of serum bilirubin previously attained or the period of disease in which exercise was given.

**328. Targan, S., L. Britvan, and F. Dorey:**

Activation of human NKCC by moderate exercise:  
Increased frequency of NK cells with enhanced capability of effector-target lytic interactions.  
*Clinical and Experimental Immunology* 45:352-360, 1981.

**Authors' abstract**

In the present study we examined the mechanism of human natural killer cellular cytotoxicity (NKCC) augmentation by 5 min of moderate exercise and its interrelationship to *in vitro* interferon (IFN) activation.

Cytotoxicity was measured by employing both a single-cell cytotoxic assay and a standard 3-hr chromium-51 (<sup>51</sup>Cr) release assay. The former was used to assess changes at the single NK cell-target cell level and the latter to assess changes in overall lytic capacity of a given population of NK cells. Several findings were obtained: (1) moderate exercise augmented NKCC *in vivo* by recruiting a "new" population of active cytotoxic NK cells. (2) This "new" population of active cells probably was derived from cells which can bind targets but are non-cytotoxic. (3) In a standard <sup>51</sup>Cr-release assay, additional augmentation of these exercise-activated cells occurred *in vitro* following exposure to interferon. (4) This additional increase in cytotoxicity produced no alteration in the frequency of killer cells as viewed at the single cell level. (5) Thus interferon's capacity to increase further the overall lytic ability of exercise-activated NK cells was not due to its activation of an additional subset of pre-NK cells, but due to its increasing the capacity of effector-target lytic interactions (recycling) of the same set of NK and pre-NK cells.

**329. Taylor, C., G. Rogers, C. Goodman,  
R.D. Baynes, T.H. Bothwell,  
W.R. Bezwoda, F. Kramer, and  
J. Hattingh:**

Hematologic, iron-related, and acute-phase protein responses to sustained strenuous exercise.  
*Journal of Applied Physiology* 62:464-469, 1987.

**Authors' abstract**

This study was undertaken to gain insight into the mechanisms responsible for the hypoferrmia occurring after severe exercise. To this end, 18 athletes who were competing in a 160-km triathlon involving canoeing, cycling, and running were evaluated before the race, immediately after the finish, and thereafter at 30 min, 24 h, and 48 h. The evaluations included plasma iron, total iron-binding capacity, lactoferrin, ferritin, haptoglobin, cortisol, various enzymes, and white cell count. The cortisol, white cell count, and lactoferrin were significantly increased immediately after the race, while the plasma iron and transferrin saturation were significantly decreased. There was a 40% but nonsignificant rise in the plasma ferritin at the completion of the race, while the C-reactive protein was raised by nearly 300% at 24 h. In contrast, haptoglobin declined significantly by 24 h but was normal again 24 h later. Quantitative considerations suggested that the lactoferrin was not responsible for removing transferrin iron from circulation and hence causing the hypoferrmia. Instead, it seemed more likely

that the iron-related changes were occurring as part of an acute phase response initiated by muscle injury.

**330. Tchorzewski, H., A. Denys, and B. Zytikiewicz:**

Sport training and some activities of human polymorphonuclear leukocyte lysosomes.  
*Zentralblatt für Bakteriologie, Mikrobiologie und Hygiene B* 162:402-407, 1976.

**Authors' Abstract**

The acid phosphatase and protease, neutral protease, bactericidal and mitogenic activities were determined in the polymorphonuclear leukocyte (PMNL) lysosomes of 16 year old boys. The investigated group consisted of 20 intense sport training persons during the last six years, the control one of the same age boys without any sport training. The significant decrease of hydrolase activity has been observed in the lysosomes of the peripheral blood PMNL's of the sport training boys.

**331. Tchorzewski, H., R. Lewicki, and E. Majewska:**

Changes in the helper and suppressor lymphocytes in human peripheral blood following maximal physical exercise.

*Archivum Immunologiae et Therapiae Experimentalis* 35:307-312, 1987.

**Authors' abstract**

Lymphocyte subpopulations and Con A activated suppressors were measured before, immediately after maximal physical effort on a bicycle ergometer and after two-hour recovery. The investigations were performed on healthy male volunteers, trained male and female cyclists, nearly at the same age. The measured parameters of maximal effort were comparable in all investigated groups. The significant increase in T8<sup>+</sup> (suppressor cytotoxic) cells and moderate increase in T4<sup>+</sup> (helper inducer) cells was observed after maximal physical effort; these changes were accompanied by a significant diminution of a T4<sup>+</sup>/T8<sup>+</sup> ratio. Two-hour recovery resulted in the normalization of the investigated parameters. The functional test based on Con A-induced suppressor activity has revealed the divergence, a decrease in Con A-induced suppressor cell activity was noted after maximal effort.

**332. Telgenhoff, G. and C. Renk:**

Effect of acute exercise on lymphocyte mitogenic responses in conditioned and non-conditioned male subjects.

*Medicine and Science in Sports and Exercise* 21:S110, 1989.

**Authors' abstract**

Ten conditioned and ten non-conditioned male subjects were evaluated for immune reactivity before and after an acute exercise regime. Subjects were divided into conditioned categories based on exercise schedule, body composition and resting heart rate. The procedure was explained to each volunteer and informed consent was obtained from each participant. Subjects were instructed to refrain from exercising 24 hrs before testing. At the beginning of each session resting heart rate and body composition were determined. Blood was then drawn immediately before initiating the exercise routine (T1). Each individual was instructed to exercise on a bicycle ergometer at a rate or tension to bring his heart rate to 75% of maximal. Once achieved, the clock was started and he was instructed to continue at this pace for the 15 min by continuous heart rate monitoring. Blood samples were drawn immediately after the 15 min session (T2) and both samples were evaluated. The results from this study show that lymphocyte function as determined by response to mitogenic stimulation was lower at T1 in the conditioned group vs the non-conditioned group. In addition, a significant depression in lymphocyte responsiveness to the mitogens, PHA, Con A, and PWM was observed at T2 vs T1 in the conditioned group. No significant effects of acute exercise were observed in the non-conditioned group. The results from this study indicate that lymphocytes from conditioned subjects are less responsive to stimulation and are suppressed after an acute bout of exercise compared to non-conditioned controls. These results suggest a role of exercise in the susceptibility of athletes to infection.

**333. Tharp, G.D. and M.W. Barnes:**

Reduction of immunoglobulin-A by swim training.  
*Medicine and Science in Sports and Exercise*  
21:S109, 1989.

**Authors' abstract**

This study examined the effect of acute and chronic exercise on the saliva immunoglobulin-A (IgA) levels of a university swim team (21 men and 18 women). Saliva samples were collected before and after two hour training sessions four times during the Fall season when the training intensity level was light (Sept), moderate (Oct), heavy (Nov), and during the taper period (Dec) before a major competitive meet. IgA was measured using a standard ELISA technique. The pre and post-session IgA

level ( $\mu\text{g/ml}$ ) at the four training intensity levels was as shown below for the women's and men's swim teams.

IgA levels were significantly decreased after each training session for the women. IgA was also reduced after each session for the men but only the moderate intensity change was statistically significant. Over the three month training period the pre-session IgA levels decreased significantly from the light to moderate to heavy intensities (women), and from the moderate to the heavy and taper intensities (men). These results indicate that acute exercise bouts can reduce saliva IgA levels and that chronic exercise of high intensity can reduce the resting levels of IgA. These changes may render the athlete more vulnerable to respiratory infections after exercise and even at rest during the later stages of the competitive season.

	<b>Light</b>	<b>Moderate</b>	<b>Heavy</b>	<b>Taper</b>
Women	239-194	182-144	138-110	184-154
Men	234-212	239-218	171-158	183-173



**334. Tharp, G.D. and M.W. Barnes:**

Reduction of saliva immunoglobulin levels by swim training.

*European Journal of Applied Physiology* 60:61-64, 1990.

**Authors' abstract**

Saliva immunoglobulin A (IgA) and cortisol levels were measured in 21 male members of a major midwestern swim team. Saliva samples were collected before and after training sessions four times during the fall season; the training intensity was light, moderate, heavy and during the taper period before a major competitive meet. Saliva IgA levels were decreased after each training session, reaching statistical significance with the moderate training intensity. Over the 3-month training period the pre-session and post-session IgA levels both decreased significantly during the heavy and taper training intensities later in the fall season. Cortisol levels were significantly elevated only after the heavy-intensity training session. The Profile of Mood States (POMS) was used to assess the swimmers' overall mood on each test day. No significant correlations were found between the global POMS score and IgA or cortisol. Also, cortisol and IgA were not significantly correlated except after the light training session. Results from this study indicate that acute bouts of exercise can reduce salivary IgA levels and that chronic exercise of high intensity can reduce the resting levels of IgA. These changes may render the athletes more vulnerable to respiratory infections after exercise and even at rest during the later stages of the competitive season.

**335. Tharp, G.D. and T.L. Preuss:**

Mitogenic response of T-lymphocytes to exercise training and stress.

*Journal of Applied Physiology* 70: 2535-2538, 1991.

**Authors' abstract**

The impact of exercise training and stress on the immune response was examined by measuring the mitogenic response of spleen lymphocytes to the T-cell mitogen concanavalin A (Con A). Male Sprague-Dawley rats were divided into four groups: sedentary controls (n = 11), handled controls (n = 12), treadmill runners (n = 10), and voluntary runners (n = 11) housed in running wheels. The treadmill group ran at 22 m/min (0.8 mph) for 45 min, 5 days/wk for 8 wk. After the training period, spleen lymphocytes isolated from each rat were incubated with Con A for 54 h, pulsed with radio-labeled thymidine for 18 h, and counted for tritium activity. Counts per minute per group ( $\bar{X} \pm \text{SE}$ ) were as follows: sedentary, 6,839  $\pm$  1,461; handled, 8,959  $\pm$  1,576; voluntary runners,

13,126  $\pm$  2,069; and treadmill runners, 18,950  $\pm$  5,975.

One-way analysis of variance and Tukey's highly significant difference test found the counts per minute of the treadmill runners to be significantly different from the counts per minute of the sedentary animals. These results indicated that the responsiveness of spleen lymphocytes to Con A increases as the level of stress and exercise increases.

**336. Thompson, H.J., A.M. Ronan,**

**K.A. Ritacco, A.R. Tagliaferro, and**

**L.D. Meeker:**

Effect of exercise on the induction of mammary carcinogenesis.

*Cancer Research* 48:2720-2723, 1988.

**Authors' abstract**

Although data reported in several epidemiological investigations indicate that reduced consumption of dietary fat and increased levels of physical activity are associated with reduced risk for breast cancer, the results of some studies do not support these observations.

Underlying this situation is the unanswered question about whether degree of body fatness, which is affected by dietary composition, total caloric intake, and energy expenditure, is the critical determinant affecting breast cancer risk. The objective of this work was to establish whether increasing energy expenditure by exercise would reduce the occurrence of mammary carcinomas induced by 7,12-dimethylbenz[a]anthracene (DMBA) in animals consuming a high fat diet to the level of occurrence observed in sedentary animals consuming a low fat diet.

Female Sprague-Dawley rats were obtained at 21 days of age and maintained on a 5% (w/w) corn oil diet (AIN-76A) until they were 64 days of age. At 50 days of age, rats received either 5 mg DMBA or the solvent in which the carcinogen was dissolved. Fourteen days after DMBA intubation they were randomized into one of three groups: 5% fat (w/w), sedentary; 24.6% fat (w/w), sedentary; or 24.6% (w/w), exercised. Animals were exercised on a motor-driven treadmill at a belt speed of 20 m/min and a 1-degree incline for 15 min/day, 5 days/week for 18 weeks. Feeding a high fat versus a low fat diet increased the number of breast cancers induced and the rate at which they appeared in agreement with previous investigations. However, rather than retarding the development of tumors as was hypothesized, moderate treadmill exercise increased the incidence and number of cancers induced and shortened cancer latency in comparison to animals that received either the high fat or low fat diet and were sedentary. Body composition was not altered by the exercise regime imposed, although these animals weighed more than either sedentary group. These

data document a heretofore unreported effect of a moderate level of aerobic work on breast cancer induction.

**337. Tilles, J.G., S.H. Elson, J.A. Shaka, W.H. Abelmann, A.M. Lerner, and M. Finland:**

Effects of exercise on Coxsackie A9 myocarditis in adult mice.

*Proceedings of the Society for Experimental Biology and Medicine* 117:777-782, 1964.

**Authors' abstract**

A cardiotropic strain of Coxsackie A9 virus was inoculated intraperitoneally into groups of adult C<sub>3</sub>H mice, one half of which were vigorously exercised daily by swimming. Uninfected controls were studied in parallel. Among the infected mice, the virus was isolated in higher titer from the hearts of a significantly greater proportion of those that were exercised. The possible mechanisms by which exercise could augment replication of the virus in the myocardial tissue were discussed. On the ninth day after inoculation, the weight and relative weight of the heart were significantly greater in the exercised mice than in those that were not exercised. Among the exercised animals, the weight and relative weight of the heart were significantly greater than in those that were not infected. The increase in weight could not be attributed to increased water content or to inflammatory infiltrate.

**338. Tomasi, T.B., F.B. Trudeau, D. Czerwinski, and S. Erredge:**

Immune parameters in athletes before and after strenuous exercise.

*Journal of Clinical Immunology* 2:173-178, 1982.

**Authors' abstract**

Secretory IgA levels were studied in nationally ranked Nordic skiers before and after the national cross-country races held in February, 1981. Comparing the skiers with age-matched controls, there was a significantly lower level of salivary IgA before the race. Concentrations of IgA decreased further following the competition (50 km for males; 20 km for females) to very low levels. There also was a significant increase in the percentage of B lymphocytes and a decrease in the null population (non-T, non-B) in the athletes after the race compared with the controls. The mechanism responsible for these changes is unknown, but the low salivary IgA levels may result from depletion of nasal fluid and/or malfunction of the mucosal plasma cells due to a decreased temperature in the mucosal membranes. We speculated that a tem-

porary antibody deficiency on the mucosal surface might lead to a susceptibility to acquiring viral and bacterial infections, especially during the interval immediately following strenuous exercise.

**339. Tuttle, W.W.:**

The effect of exercises of graded intensity on the leukocyte count.

*Research Quarterly* 6:37-45, 1935.

**Synopsis**

**Purpose** To determine the relationship between the severity of exercise and the number of leukocytes in circulating blood.

**Methods**

1. Blood was drawn from a fingertip and counted twice using a hemocytometer.
2. Six stool-stepping exercise routines of graded intensity, the last being the most strenuous, were employed and blood collected within first 10 seconds of exercise completion.
3. Leukocyte counts were done under basal conditions, normal activity, and after the six exercises of graded intensity.

**Results**

1. In every case except one, the leukocyte count after the sixth exercise was greater than at any other time during the experiment.
2. Increase in the leukocyte count had a tendency to follow the heart rate increase.

**Conclusions**

1. Exercise, within the limits of this study, causes an increase in the number of leukocytes in the circulating blood. This increase varies directly with the severity of the exercise.
2. The number of leukocytes in the circulating blood varies directly with heart rate suggesting that leukocytosis due to exercise is probably caused by the washing out of the cells from areas which tend to be stagnant, thus bringing them into the peripheral circulation.
3. No evidence suggests the possibility of inflammatory leukocytosis due to exercise.

**340. Tvede, N., C. Hellmann, J. Halkjær-Kristensen, and B.K. Pedersen:**

Mechanisms of B-lymphocyte suppression induced by acute physical exercise.

*Journal of Clinical and Laboratory Immunology* 30:169-173, 1989.

**Authors' abstract**

Blood mononuclear cells from 20 healthy untrained volunteers were isolated before, during, 2 hr and 24 hr after bicycle exercise at 80% of  $\dot{V}O_2$  max for 1 hr. A reverse plaque forming cell assay was used to investigate B-lymphocyte function. Stimulation with pokeweed mitogen, recombinant interleukin 2 and Epstein-Barr virus resulted in significant decreases in numbers of IgG-, IgM-, and IgA-secreting blood cells during as well as 2 hr after exercise, with reversal to pre-exercise values 24 hr later. During and after physical activity we found an unchanged concentration of CD20-positive B lymphocytes suggesting that the suppression of immunoglobulin secreting cells was not due to changes in numbers of B lymphocytes. A decline in CD4/CD8 ratio was measured only during exercise with normalization after exercise. Therefore the B-lymphocyte suppression, most pronounced 2 hr after exercise, was presumably not due to changes in T lymphocytes also indicated in the experiments using EBV-stimulated cultures since EBV act directly on B lymphocytes. Two hours after physical activity an increased level of CD14-positive monocytes were observed and the monocytes expressed higher levels of surface HLA-DR during as well as 2 hr after exercise. Addition of indomethacin caused an increased response only in the IL-2 stimulated cultures, suggesting that IL-2 sensitive activated B lymphocytes are downregulated by prostaglandins. Purified B lymphocytes produced plaques only after EBV-stimulation, and in these cultures no exercise-induced suppression was found, likewise suggesting an inhibitory effect of the activated monocytes.

**341. Tvede, N., B.K. Pedersen, F.R. Hansen, T. Bendix, L.D. Christensen, H. Galbo, and J. Halkjær-Kristensen:**

Effect of physical exercise on blood mononuclear cell subpopulations and in vitro proliferative responses.

*Scandinavian Journal of Immunology* 22:383-389, 1989.

**Authors' abstract**

The present study was designed to examine the effect of physical exercise on subsets and proliferative responses of blood mononuclear cells. Sixteen young, healthy volunteers underwent 60 min of bicycle exercise at 75% of maximal oxygen uptake ( $\dot{V}O_2$  max). After an interval of at least 1 week, six of the subjects underwent a 60-min back muscle training period at up to 30% of  $\dot{V}O_2$  max. Blood samples were collected before and during the last minutes of exercise, as well as 2 and 24 h later. Blood mononuclear cell (BMNC) subpopulations were determined and the proliferative responses after incubation with phytohemagglutinin (PHA) or purified derivative of tuberculin (PPD), were quantified by [ $^3$ H] thymidine incorporation. During bicycle exercise the relative blood concentration of T cells (CD3<sup>+</sup> cells) declined, mainly due to a fall in T helper cells (CD4<sup>+</sup> cells). The natural killer (NK) cell subset (CD16<sup>+</sup> cells) increased during work, but reverted after; the monocytes (CD14<sup>+</sup> cells) increased 2 h after work, whereas the B-cell subset (CD20<sup>+</sup> cells) did not change. BMNC subsets were not significantly changed by back muscle exercise. The PHA-induced proliferative response decreased during bicycle exercise, whereas the PPD-induced response did not change. No significant changes occurred during back muscle exercise. Investigation of subgroups after incubation with [ $^3$ H] thymidine showed that the proliferative response per CD4<sup>+</sup> cell did not change in relation to exercise, but the contribution of the CD4<sup>+</sup> subgroup to proliferation declined during bicycle exercise due to the decreased proportion of CD4<sup>+</sup> cells. The suppression of the PHA response during bicycle exercise can be explained in part by a relative fall in CD4<sup>+</sup> cells. The pool sizes of BMNC subfraction may be elicited by increased catecholamine and cortisol levels.

### 342. Uhlenbruck, G. and U. Order:

Can endurance sports stimulate immune mechanisms against cancer and metastasis?  
*International Journal of Sports Medicine*  
12:S53-S68, 1991.

#### Authors' abstract

Proceedings from a brief historical contemplation of the problematic nature of "exercise and malignancy" a training investigation (running on a treadmill) with animals is presented. By means of the experimental tumor model fibrosarcoma L-1 of BALB/c mice differences in growth, size, and metastatic spreading have been proven depending upon the mode and more significantly on the intensity of training and upon the mode of application and inoculation of tumor cells. Accordingly the best cancer-protective effect could be observed when the animals performed a pre- and a post-running training before and after inoculation. Moreover, mechanisms of the acute phase response of human athletes are discussed in relation to possible prophylactic effects on the prevention of infections and on the development of cancer.

### 343. Vena, J.E., S. Graham, M. Zielezny,

J. Brasure, and M.K. Swanson:  
Occupational exercise and risk of cancer.  
*American Journal of Clinical Nutrition* 45:318-327, 1987.

#### Authors' abstract

This paper briefly summarizes previously published findings and examines the relationship between physical activity on the job and occupational mortality in Washington State for the digestive cancers. It also includes information on other cancers that could be related to energy expenditure (EE) and/or obesity, as well as preliminary findings from the Western New York Diet Study on the relationship between occupational physical activity and potential risk factors and confounding variables for cancer, including demographics, habits such as consumption of alcohol and smoking, detailed dietary measures, bowel habits and medical history.

### 344. Verde, T.J.:

The effects of acute exercise and heavy training on immune function in elite athletes.  
*Doctoral Dissertation: University of Toronto,*  
Canada: 1990. 232 p.

#### Author's abstract

The study was designed to investigate the effects of acute exercise and heavy training on immune function

in elite athletes. Ten elite male runners (mean age =  $29.8 \pm 1.7$  yr; mean  $\dot{V}O_2$  max  $+65.3 \pm 4.9$  ml/kg·min; mean personal best 10 km race time =  $31:43 \pm 1$  min 46 sec) volunteered to participate. Each subject was evaluated immediately before, immediately after, and 21 days after a three-week-period of heavy training. On average the heavy training constituted a 38% increase in training volume over their typical weekly training regimens. At each laboratory evaluation, the subjects ran for 30 minutes on a treadmill at 80% of their  $\dot{V}O_2$  max. Venous blood samples were taken before, 5 minutes after and 30 minutes after the bout of acute exercise. The specific *in vitro* measurements of immune function chosen for this study were phytohaemagglutinin (PHA) and concanavalin A (Con A) stimulation of lymphocyte proliferation; production of immunoglobulins IgG and IgM by lymphocytes stimulated with pokeweed mitogen; and an assessment of the subpopulations of T-cells present in peripheral blood. Following three weeks of heavy training, blood samples taken at rest indicate trends for an increased rate of proliferation, a decreased production of the immunoglobulins IgG and IgM, and a decreased ratio of helper cells (H) to suppressor cells (S). Immediately following heavy training, thirty minutes of submaximal treadmill running resulted in a significant 17.9% suppression of PHA-induced lymphocyte proliferation and a similar but not statistically significant 11.7% suppression of Con A-induced lymphocyte proliferation. Recovery from the suppression was not complete within thirty minutes of ceasing exercise. In contrast, three weeks of heavy training did not result in a significant exercise-induced suppression of immunoglobulin synthesis. Thirty minutes of maximal exercise resulted in a significant decrease of the H/S ratio only at the final testing session. The observed exercise-induced decrease in ratio was not significant immediately before or immediately after the three weeks of heavy training. The data suggest that the observed impact of heavy training on immune function in athletes is dependent on the chosen *in vitro* measure of immune function. While resting cell-mediated lymphocyte function (as assessed by *in vitro* proliferation) seemed to be enhanced with heavy training, cell-mediated immunosurveillance (as measured by H/S ratio) and humoral antibody production seemed to be impaired. On the other hand, heavy training resulted in significant exercise-induced suppression of cell-mediated lymphocyte function, a suppression which was not confirmed by the other two measurements of immune function. The clinical significance of the observed alterations of immune measures in the athletes remains to be determined.

**345. Verde, T.J., S.G. Thomas, and R.J. Shephard:**

Influence of heavy training on immune response to acute exercise in elite runners.  
*Medicine and Science in Sports and Exercise*  
21:S110, 1989.

**Authors' abstract**

Ten elite runners (age =  $29.8 \pm 1.7$  years;  $\dot{V}O_{2\max} = 65.3 \pm 4.9$  ml/kg/min.; personal best 10 k. time =  $31:43 \pm 1:46$  min.) were evaluated before and after 3 weeks of heavy training. On average the heavy training constituted a 47% increase over baseline training load. Before and after the 3 weeks of heavy training each runner ran for 30 min. on a treadmill at 80% of their  $\dot{V}O_{2\max}$ . Venous blood was sampled before and 5 min. following the treadmill run. Mitogen induced proliferation of peripheral blood mononuclear cells was used as an assessment of immune function. The heavy training load did not alter  $\dot{V}O_{2\max}$  (pre  $\bar{X} = 65.3$ , post  $\bar{X} = 65.1$ ). There was no difference in mitogen induced cell proliferation in resting blood sampled before and after heavy training. Acute exercise (REST proliferation - 5 POST proliferation) did not suppress immune function before heavy training but the acute exercise challenge significantly ( $P < 0.05$ ) suppressed immune function following the 3 weeks of heavy training.

**346. Viti, A., M. Muscettola, L. Paulesu, V. Bocci, and A. Almi:**

Effect of exercise on plasma interferon levels.  
*Journal of Applied Physiology* 59:426-428, 1985.

**Authors' abstract**

The effect of exercise on plasma interferon activity was studied on eight male subjects before and after exercise on a bicycle ergometer for 1 h at 70% of their maximal  $O_2$  consumption ( $\dot{V}O_{2\max}$ ). Acid-labile interferon,  $\alpha$ -type according to immunological characterization, rose significantly from a preexercise value of  $3 \pm 1$  to  $7 \pm 2$  IU/ml postexercise. Negligible changes were recorded for plasma protein, lipid and glucose concentrations, whereas blood lactate slightly increased only at the end of exercise. According to hematocrit and plasma protein values before and after exercise, hemoconcentration did not occur. These data provide evidence that plasma interferon activity increased following a bout of submaximal exercise.

**347. Von Weiss, M., J. Fuhmanský, R. Lulay, and H. Weicker:**

Häufigkeit und Ursache von Immunglobulinmangel bei Sportlern.  
*Deutsche Zeitschrift für Sportmedizin* 36:146-153, 1985.

**Authors' abstract**

In a more than two year period we measured immunoglobulin concentrations (IgG, IgA, IgM) in 953 sportsmen paralleled with data about infectious diseases and training, and tested the maximal performance on a bicycle ergometer or a treadmill. At the time close before examination 14.1% of the sportsmen have had febrile infections, anamnestic data showed in 11.8% severe bacterial and/or viral infectious, diseases formerly, and 9.2% had atopic diseases. 89.9% of the sportsmen showed IgA values below the middle values of the control group and 12.3% below the normal range, 2% showed subnormal values of IgM and 5.4% of IgG. IgA increases with age, and IgM showed differences between males and females. Sportsmen with tonsillectomy and more than two children's diseases showed lower IgA levels than such without tonsillectomy or less than two children's diseases. By a questionnaire we revealed that the social field in childhood, nutrition during training period and perhaps some forms of training induced the levels of IgA, but they did not depend on the intensity or extensity of training or the time since starting the sporting activity. In agreement with literature we could show that hard training or overload is able to influence the immunological reaction. Therefore, one should pay attention to the immunological status examining especially young sportsmen.

**348. Voronina, N.P., and D.N. Mayanskii:**

Effect of intensive physical exercise on macrophagal functions.  
*Bulletin of Experimental Biology and Medicine*  
104:1120-1123, 1987.

**Authors' abstract**

The functional state of phagocytic cells of the reticuloendothelial system (RES) and, in particular, its chief compartment—the mononuclear phagocytic system (MPS)—essentially determine resistance to trauma, blood loss, burn toxemia, various forms of circulatory shock, and so on. After treatment of animals with various substances stimulating RES function (microaggregated human albumin, glyceryl trioleate, quinones, a combination of estrogens and glucocorticoids), in many cases tolerance to stress increased, whereas after blockade or depression of the phagocytic activity of the resident macrophages (mph), mortality increased. It was shown

previously that after sudden cooling (to  $-7^{\circ}\text{C}$ ), acute physical exercise, and administration of hydrocortisone in a dose of 125 mg/kg, the clearing function of the RES was abruptly depressed, with a corresponding lowering of resistance to stress; the ingestive function of the RES was depressed after acute stress, moreover, because of depression of the phagocytic function of the Kupffer cells (KC) of the liver, whereas clearance of the blood of pulmonary interstitial Mph showed a compensatory increase. Meanwhile, the functional activity of Mph from different compartments of the MPS during stress has received little study.

### 349. Wake, R.F., B.F. Graham, and S.D. McGrath:

A study of eosinophil response to exercise in man. *Aviation Medicine* 24:127-130, 1953.

#### Synopsis

**Purpose** To study the eosinophil response to exercise.

#### Methods

1. 21 members of R.C.A.F. ground crew in groups of six or less were observed over two periods of 12 hours, from 8:00 a.m. to 8:00 p.m.
2. During one period, subjects were kept physically active with games such as basketball, bowling, and badminton.
3. During the other period, subjects were kept at rest on beds and only got up for meals.

4. During these periods, blood was taken from the ears at 2-hourly intervals and the number of circulating eosinophils was counted.

#### Results

1. The means of the starting counts were substantially the same on both days.
2. The mean of the decrease between 8:00 a.m. and 10:00 a.m. on the exercise day was greater than on the rest day, but the difference between these means was not significant.

3. The changes from the starting count on the exercise day were significantly lower from those after corresponding intervals on the rest day.

#### Conclusions

1. Exercise of this order causes activation of the adrenal cortex.

### 350. Watson, R.R., S. Moriguchi, J.C. Jackson, L. Werner, J.H. Wilmore, and B.J. Freund:

Modification of cellular immune functions in humans by endurance exercise training during  $\beta$ -adrenergic blockade with atenolol or propranolol. *Medicine and Science in Sports and Exercise* 18:95-100, 1986.

#### Authors' abstract

Young healthy previously inactive men were trained aerobically 40 to 50 min/d, 5 d/wk for 15 wk. They were randomly assigned to one of three medication groups: placebo, propranolol (160 mg/d), or atenolol (100 mg/d). All subjects lost weight and decreased relative body fat as a result of training. Following training, submaximal steady-state heart rates were reduced in all groups. Maximal oxygen uptake and maximal treadmill times were also increased in all groups. The  $\text{VO}_2\text{max}$  of the placebo increased 18.4%. While that of the atenolol group increased 19.4%, the propranolol group went up 17%. After training the maximal heart rate did not change in the placebo group, while treatment with propranolol and atenolol reduced it 24.6 and 21.9%, respectively. Training caused a significant decrease in the natural killer cell activity in all three groups. The placebo group had  $38.8\% \pm 3.8$  (SD) before and  $29.3 \pm 3.2\%$  lysis of target cells by natural killer cell activity after physical conditioning, which was significantly lower ( $P < 0.01$ ). The groups treated with propranolol and atenolol were also similarly decreased. The use of propranolol or atenolol had no additional significant effect on natural killer cell activity. T-cell mitogenesis stimulated with a mitogen significantly increased with conditioning. The groups given atenolol or propranolol tended to increase somewhat more than the placebo group, although this difference was not statistically significant. There was no significant change in the percentage of total lymphocytes due to training or  $\beta$ -blockade. The number of mature T-lymphocytes measured by the E-rosetting technique increased significantly consequent to physical conditioning, with propranolol and/or atenolol having no additional effect. The placebo group had  $65 \pm 1.3\%$  of lymphocytes as T-lymphocytes before and  $74 \pm 1.4\%$  after conditioning ( $P < 0.05$ ). The increased percentage of lymphocytes which formed E-rosettes (mature T-lymphocytes) occurred as activity of the natural killer cells declined. This suggests that exercise training may influence the maturation and/or function of cells of the cellular immune system.

**351. Weicker, H. and E. Werle:**

Interaction between hormones and the immune system.

*International Journal of Sports Medicine*  
12:S30-S37, 1991.

**Authors' abstract**

After a short introduction into the general topic, the catecholamine-induced increase of leukocytes in which the granulocytes are predominant after short-term exercise is discussed. The reduction of lymphocytes is associated with work-dependent cortisol increase after long-term exercise or 1 hr of strenuous work. The catecholamine-stimulated lymphocytes increase could be explained by the liberation of the cells from the endothelial vessel wall after catecholamine interaction with the  $\beta$ -adrenoceptors and by mobilization from lymph nodes and spleen after  $\beta$ -adrenergic stimulation. Catecholamines reduce the proliferation of lymphocytes and the degranulation of mast cells, preventing hypersensitivity reaction due to inhibited mediator liberation. The influence of cortisol on cytokines and vice versa is discussed. The hormonal changes after runs of different intensities and duration are demonstrated; they show an interaction with immunological regulation. The neuro-immune modulation after physical and psychological stress also has to be considered in immune regulation since under this condition the secretion of encephalins, endorphins, ACTH, and cortisol is increased. The significance of enhanced vasopressin secretion causing postural fainting by vagovasal reaction indicates also the effect of a neuropeptide which is related to immunological reactions. In the changes of lymphocyte subclasses, the homing effect of these cells should be regarded. Advice which can improve the immunologic behavior, avoiding susceptibility to infections by well-conducted training regimens and adequate periods of regeneration time, are necessary. The multifold mechanisms involved in the immune regulation and the interaction with several hormonal and metabolic changes caused by exercise make it difficult to give, at the present time, well-founded practical pieces of advice; it needs more work and well-conducted studies of exercise and competition.

**352. Wells, C.L., J.R. Stern, and L.H. Hecht:**

Hematological changes following a marathon race in male and female runners.

*European Journal of Applied Physiology* 48:41-49, 1982.

**Authors' abstract**

The subjects of this experiment were well-trained men (6) and women (4) participating in a marathon race in Phoenix, Arizona, on a cool, cloudy, windy day. Venous blood was collected one week prior to the run, immediately after, and 4, 8, and 24 h after the race. There were no significant changes in hematocrit, hemoglobin, or red blood cell counts following the race. The sample collected immediately after the race showed a pronounced leukocytosis. Differential counts showed that this increase in white blood cell count was limited to polymorphonuclear cells, suggesting that an inflammatory response to stress of the race was involved. Percentage changes in blood volume, red blood cell volume, and plasma volume were calculated from hematocrit and hemoglobin changes. These changes showed that there was reduction of plasma volume of 8% for females and 13% for males immediately after the race, with return to initial values within 8 h. We suggest that the increase in protein following the race was contributed by the flow of lymph from muscle to the vascular compartment.

**353. Wilkerson, J.E., M.A. Kolka and**

**L.A. Stephenson:**

Exercise induced leukocytosis during a competitive marathon.

*Medicine and Science in Sports and Exercise* 11:99, 1979.

**Authors' abstract**

Three adult male volunteers ran a competitive marathon (42.2 km) with a catheter in a cubital vein. Blood samples were drawn every 4.8 km (3 mi) during the race. In each sample, the whole blood hemoglobin (Hb) concentration, and the hematocrit (Hct) were measured and erythrocyte (EC) and leukocyte (LC) counts were made. EC decreased by an average of 1.50% during the race from pre-race control levels of 5.68 million cell/mm<sup>3</sup>. Hb increased by 8.09% and Hct decreased by an average of 2.82% during the race. Mean corpuscular volume increased by 2.60% with an 11.11% increase in mean corpuscular hemoglobin. There was a linearly increasing leukocytosis throughout the race such that by 38.6 km (24 mi) LC averaged 17,850 cells/mm<sup>3</sup>, an increase of 285.3% above pre-race control LC. The leukocytosis was the result of an increase in the absolute number of circulating white blood cells since plasma volume only

decreased by 4.44% during the race (calculated from HB and Hct). Contrary to previous reports of exercise leukocytosis, LC was still elevated one hour post race (average  $LC = 16,533 \text{ cells/mm}^3$ ) suggesting a combination of margination (physiological neutrophilia) and febrile responses.

**354. Williams, R.S., R.S. Eden, M.E. Moll, R.M. Lester, and A.G. Wallace:**

Autonomic mechanisms of training bradycardia:  $\beta$ -adrenergic receptors in humans.  
*Journal of Applied Physiology* 51:1232-1237, 1981.

**Authors' abstract**

To address the autonomic mechanism underlying the bradycardia of physical training in human subjects, we performed a cross sectional study comparing the heart-rate responses to graded doses of isoproterenol in 7 elite marathon runners and 7 age-matched controls, and a longitudinal study in 12 normal volunteers of the effects of 6 wk of intense physical training on lymphocyte  $\beta$ -adrenergic receptors identified by  $l$ -[ $^3\text{H}$ ]dihydroalprenolol. We observed no significant difference between marathoners and controls in the dose of isoproterenol that produced a 25-beat/min increment in heart rate, either in the absence ( $1.9 \pm 0.6$  vs.  $2.5 \pm 0.6 \mu\text{g}$ ;  $P, 0.509$ ) or in the presence of cholinergic blockade ( $4.4 \pm 1.3$  vs.  $3.1 \pm 0.4 \mu\text{g}$ ;  $P, 0.320$ ). Likewise, we observed no effects of physical training on lymphocyte  $\beta$ -adrenergic receptors in terms of receptor affinity ( $K_d$   $4.0 \pm 0.7$  vs.  $3.6 \pm 0.7 \text{ nM}$ ) ( $P, 0.9178$ ). Although our data cannot exclude reduced chronotropic sensitivity to catecholamines as contributing to lowered heart rate in some highly conditioned individuals, these results are consistent with the hypothesis that altered neuronal input to the sinus node is usually a more important mechanism of training bradycardia.

**355. Wit, B.:**

Immunological response to physical effort.  
In: *International Perspectives in Exercise Physiology*, edited by K. Nazar, R.L. Terjung, H. Kaciuba-Uscilko, and L. Budohoski.  
Champaign, IL.: Human Kinetics Books, 1990.  
p. 220.

**Author's abstract**

In the present study the following problems were examined: to what extent regular training affects the responses of immunological resistance measured at a cell level; whether the training load applied to athletes disturbs their humoral resistance; and whether the level of immuno-

globulins changes during the training cycle in systematically training athletes. This study included 217 athletes of four sport disciplines and four control groups. In distance runners, cell resistance tests and humoral resistance tests were performed (lymphocyte transformation test-LTT, migration inhibition test-MIT, T, and B lymphocyte counts, as well as concentrations of immunoglobulins IgG, IgA, and IgM). In gymnasts, canoeists, and swimmers the immunoglobulin level (IgG, IgA, IgM) was determined in NOR-Partigen plates. In gymnasts, measurements were repeated three times in 12-month intervals, whereas in canoeists and swimmers they were performed during various periods of the training cycle. Similar measurements were also made in the control groups. More pronounced changes occurred in the humoral resistance parameters as compared to those in the cell resistance indicators. A decrease in the immunoglobulin level to the lower limits of physiological values was noted at the period of competitions and just prior to it. One should also note the nonspecific activation of the immunological system during the intermediate periods of the training cycle.

**356. Xusheng, S., X. Yuqi, Z. Rongguang, and S. Li:**

Preliminary study on immunity in ballet dancers.  
*Canadian Journal of Sport Sciences* 13: 33P, 1988.

**Authors' abstract**

The peripheral blood samples obtained from 32 ballet dancers with a mean of 17.5 years and 32 age-matched non-dancers who comprised a control group were analyzed by using the microdeterminations of lymphocyte blast transformation and mixture rosette forming cells. The percentage of lymphocyte blast transformation of ballet dancers was normal, but their percentage of E-rosette forming cells was lower than that of controls at rest. A significant increase of the percentage of zymosan-complement rosette forming cells was found during dancing. The present study suggests that a saving effect on expenditure of cellular immunofunction is exhibited in ballet dancers at rest and that the intensive ballet-exercise induces an immediate humoral immune response change. However, the effect needs to be dynamically observed and the clinical implication of the response change remains to be proved.



**357. Xusheng, S., X. Yugi, and X. Yunjian:**

Determination of E-rosette-forming lymphocytes in aged subjects with Taichiquan exercise.

*International Journal of Sports Medicine*  
10:217-219, 1989.

**Authors' abstract**

T-lymphocytes were determined by rosette formation with sheep erythrocytes in the peripheral blood obtained from 30 healthy aged subjects who were practicing Taichiquan (88 style) exercise and 30 age-matched normal aged who served as a control group. At rest the total number of T-lymphocytes and the number of active T-lymphocytes were increased significantly in the exercise group compared with the controls. Immediately after a bout of Taichiquan exercise, a marked increase of active T-lymphocytes occurred. In conclusion, the results indicate that frequent Taichiquan exercise causes an increase of T-lymphocytes in the blood.

**358. Yu, D.T.Y., P.J. Clements, and**

**C.M. Pearson:**

Effect of corticosteroids on exercise-induced lymphocytosis.

*Clinical and Experimental Immunology* 28:326-331, 1977.

**Authors' abstract**

Eight subjects ran on a treadmill at 8 miles per hr for 10 min. All developed lymphocytosis with predominant effect on the B cells. This was repeated 5 hr after receiving 60 mg of Prednisone. The lymphocytosis of both T and B cells was suppressed. When this was repeated 2 hr after receiving Prednisone, only lymphocytosis of the T subpopulation was suppressed. It was concluded that corticosteroid administration could suppress entry of lymphocytes into the circulation, with preponderant effect on the T subpopulation.

**359. Zaboklicki, S. and K. Zeman:**

Badania nad zdolnością redukcji białku nitrotetrazoliowego (NBT) przez granulocyty obojętnochłonne krwi obwodowej po jednorazowym wysiłku dawkowanym oraz w różnych porach dnia. (Investigation on the ability of nitroblue tetrazolium (NBT) reduction by peripheral blood neutrophil granulocytes after one graded exercise and at various times of the day).

*Polski Tygodnik Lekarski* 31:1321-1324, 1976.

**Authors' abstract**

The process of phagocytosis of bacteria causes in neutrophil granulocytes of peripheral blood intensification of metabolic activity manifested, among others, with increased uptake of glucose and oxygen and production of hydrogen peroxide. These changes cause reduction of nitroblue tetrazolium (NBT) to insoluble formazons precipitated in cells during phagocytosis. The purpose of the present work was to establish how one graded exercise and different times of the day influence the phagocytosis ability of neutrophil granulocytes in peripheral blood. The experiments carried out on 12 pugilists and 30 non-trained students demonstrated that graded exercise increased the spontaneous reduction ability of peripheral blood granulocytes, while no significant differences were found in the results of NBT tests carried out at different times of the day.

**360. Zänker, K.S. and R. Kroczek:**

Looking along the track of the psychoneuro-immunologic axis for missing links in cancer progression.

*International Journal of Sports Medicine*  
12:S58-S62, 1991.

**Authors' abstract**

The present data report on five bereaved cancer patients with initial progression free disease in respect to natural killer cell activity,  $\beta$ -endorphin binding capacity of their peripheral blood lymphocytes, and psychometrically objective parameter depression during widowhood. In bereaved and severely depressed cancer patients, there is a tendency of an earlier onset of decreased natural killer cell activity and a reduced binding affinity of  $\beta$ -endorphin to peripheral blood lymphocytes. A second set of data obtained from a cancer patient cohort study shows a correlation between the two variables depression and  $\beta$ -endorphin, profiles are inversely correlated, and cancer patients doing clinically well, state that physical activities counteract possible day-to-day depressive disorders. Taking together the two sets of data, one might speculate that for a definable subgroup of cancer patients physical activities raise endorphin levels and psychological well-being, both of which might modulate the activity of immune competent cells, which leads to an extended period of progression-free disease.

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## REPORT DOCUMENTATION PAGE

Form Approved  
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE <b>November 1993</b>	3. REPORT TYPE AND DATES COVERED Technical Memorandum
4. TITLE AND SUBTITLE  Exercise, Exercise Training, and the Immune System: A Compendium of Research (1902-1991)		
5. FUNDING NUMBERS  199-18-12-07		
6. AUTHOR(S)  Hardesty, A.J., Greenleaf, J.G., Simonson, S. *, Hu, A., *, and C.G.R. Jackson*		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)  Ames Research Center Moffett Field, CA 94035-1000		
8. PERFORMING ORGANIZATION REPORT NUMBER  A-93091		
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)  National Aeronautics and Space Administration Washington, DC 20546-0001		
10. SPONSORING/MONITORING AGENCY REPORT NUMBER  NASA TM-108778		
11. SUPPLEMENTARY NOTES  Point of Contact: John Greenleaf, Ames Research Center, MS 239-11, Moffett Field, CA 94035-1000; (415) 604-6604 *College of Health and Human Services, University of Northern Colorado, Greeley, CO 80639-0001		
12a. DISTRIBUTION/AVAILABILITY STATEMENT  Unclassified — Unlimited Subject Category 52		
12b. DISTRIBUTION CODE		
13. ABSTRACT (Maximum 200 words)  This compenium includes abstracts and synopses of clinical observations and of more basic studies involving physiological mechanisms concerning interaction of physical exercise and the human immune system. If the author's abstract or summary was appropriate, it was included. In other cases, a more detailed synopsis of the paper was prepared under the subheadings Purpose, Methods, Results and Conclusions. Author and subject indices are provided, plus a selected bibliography of related work or those papers received after the volume was being prepared for publication. This volume includes material published from 1902 through 1991.		
14. SUBJECT TERMS  Exercise, Exercise training, Immune system		
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT
15. NUMBER OF PAGES 167		20. LIMITATION OF ABSTRACT A08

